KDT 7th Edition
Problem based Questions

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INTRODUCTION, ROUTES OF DRUG ADMINISTRATION

1.1. A 5-year-old child is brought to the hospital with the complaint of fever, cough, breathlessness and chest pain. On examination he is found to be dull, but irritable with fast pulse (116/min), rapid breathing (RR 50/min) and indrawing of lower chest during inspiration, wheezing, crepitations and mild dehydration. Body temperature is 40°C (104°F). The paediatrician makes a provisional diagnosis of acute pneumonia and orders relevant haematological as well as bacteriological investigations. He decides to institute antibiotic therapy.

(a) In case he selects an antibiotic which can be given orally as well as by i.m. or i.v. injection, which route of administration will be most appropriate in this case?

(b) Should the paediatrician administer the antibiotic straight away or should he wait for the laboratory reports?

(see Appendix-1 for solution)

SOLUTION 1.1

SOLUTION 1.1

a. Since the child is seriously ill, a fast and more predictable action of the antibiotic is needed; a parenteral route of administration is appropriate. Moreover, oral dosing may be difficult in this case as the child is dull and irritable. Entering a vein for i.v. injection is relatively difficult in children, particularly in the presence of dehydration. Therefore, the antibiotic may be injected i.m. However, if an i.v. line is set up for rehydration, the antibiotic may be administered through the i.v. line.

b. In this case the provisionally selected antibiotic should be started as early as possible, because the child is seriously ill. Waiting for the lab. reports to confirm the diagnosis/select the definitive antibiotic may compromise the prognosis.

MEMBRANE TRANSPORT, ABSORPTION AND DISTRIBUTION OF DRUGS

2.1 A 60-year-old woman complained of weakness, lethargy and easy fatigability. Investigation showed that she had iron deficiency anaemia (Hb. 8 g/dl). She was prescribed cap. ferrous fumarate 300 mg twice daily. She returned after one month with no improvement in symptoms. Her Hb. level was unchanged. On enquiry she revealed that she felt epigastric distress after taking the iron capsules, and had started taking antacid tablets along with the capsules.

(a) What could be the possible reason for her failure to respond to the oral iron medication?

2.2 A 50-year-old type-2 diabetes mellitus patient was maintained on tab. glibenclamide (a sulfonylurea) 5 mg twice daily. He developed toothache for which he took tab. aspirin 650 mg 6 hourly. After taking aspirin he experienced anxiety, sweating, palpitation, weakness, ataxia, and was behaving abnormally. These symptoms subsided when he was given a glass of glucose solution.

(a) Waht could be the explanation for his symptoms?

(b) Which alternative analgesic should have been taken?

(see Appendix-1 for solutions)

SOLUTION 2.1 & SOLUTION 2.2

SOLUTION 2.1

a. Gastric acid is required for the absorption of oral iron salts. Concurrent ingestion of antacid tablets could have interfered with iron absorption. Hence, the anaemia failed to improve.

SOLUTION 2.2

a. Aspirin displaces sulfonylureas from plasma protein binding sites. Therefore, plasma concentration of unbound (and active) glibenclamide would have risen after aspirin ingestion causing hypoglycaemia which produced the symptoms. As such, glucose ingestion relieved the symptoms.
b. Paracetamol and ibuprofen are analgesics equally effective in toothache as aspirin, and do not displace or otherwise interact with sulfonylureas. As such, these analgesics are more suitable for the given patient.

METABOLISM AND EXCRETION OF DRUGS, KINETICS OF ELIMINATION

3.1 A 30-year-old mother of 2 children weighing 60 kg was taking combined oral contraceptive pill containing levonorgestrel 0.15 mg + ethinylestradiol 30 µg per day cyclically (3 weeks treatment—1 week gap). She developed fever with cough and was diagnosed as a case of pulmonary tuberculosis after sputum smear examination. She was put on isoniazid (300 mg) + rifampin (600 mg) + pyrazinamide (1.5 g) + ethambutol (1.0 g) daily for 2 months, followed by isoniazid (600 mg) + rifampin (600 mg) thrice weekly. In the 3rd month she failed to have the usual withdrawal bleeding during the gap period of contraceptive cycle. After 10 days her urinary pregnancy test was found to be positive.

(a) What could be the reason for failure of the oral contraceptive?

(b) What precaution could have prevented the unwanted pregnancy?

3.2 A 20-year-old patient weighing 60 kg has to be prescribed an antiepileptic drug (available as 200 and 400 mg tablets) for generalized tonic-clonic seizures. The pharmacokinetic parameters and therapeutic plasma concentration of the selected drug are:

Target steady-state plasma concentration (Cpss)	– 6 mg/L
Oral bioavailability (F)	– 70%
Volume of distribution (V)	– 1.4 L/kg
Clearance (CL)	– 80 ml/hr/kg
Plasma half life (t½)	– 15 hours

What should be the loading dose and the daily maintenance dose of the drug for this patient? (see Appendix-1 for solutions)

SOLUTION 3.1

SOLUTION 3.1

a. Rifampin is known to induce the metabolism of contraceptive steroids. Thus, after regular intake of rifampin for more than 2 weeks (needed for enzyme induction) the steady-state blood level of levonorgestrel and ethinylestradiol could have fallen below the threshold for inhibition of ovulation/contraception. As such, fertility was restored and the woman conceived.

b. In view of the essentiality of rifampin (and other antitubercular drugs) in this patient and the likelihood of failure of the oral contraceptive, the couple should have been advised to take additional/alternative contraceptive measure such as condom or intrauterine contraceptive device.

SOLUTION 3.2

SOLUTION 3.2

The total volume of distribution and total body clearance for this patients has to be calculated first.

Total V = 1.4 L/kg × 60 kg = 84 L

Total body clearance (CL) = 80 ml/hr/kg × 60 kg

= 4.8 L/hr

Fractional bioavailability (F) $= \frac{70}{100} = 0.7$

Applying the formula:

Loading dose $= \frac{\text{target Cp} \times \text{V}}{\text{F}}$

Or $\frac{6 \text{ mg/L} \times 84 \text{ L}}{0.7} = 720 \text{ mg}$

Maintenance dose rate $= \frac{\text{Cpss} \times \text{CL}}{\text{F}}$

Or $\frac{6 \text{ mg/L} \times 4.8 \text{ L/hr}}{0.7} = 41 \text{ mg/hr}$

Or $41 \text{ mg/hr} \times 24 \text{ hr} = 984 \text{ mg/day}$

For this patient: Loading dose 720 mg initially; or practically 3½ tablets of 200 mg each.

Maintenance dose: 984 mg/day.

To be practical, the maintenance dose could be one 400 mg tab. in the morning and 1½ tab. (600 mg) in the evening.

MECHANISM OF DRUG ACTION; RECEPTOR PHARMACOLOGY

4.1 A patient being treated with methotrexate (Mtx) developed oral ulceration, megaloblastic anaemia and other toxic symptoms. Given that (i) Mtx acts by inhibiting the enzyme dihydrofolate reductase (DHFRase) which generates the essential coenzyme tetrahydrofolic acid (THFA) from dihydrofolic acid (DHFA) needed for one carbon transfer reactions, (ii) Mtx binds to the catalytic site of DHFRase with an affinity 50,000 times greater than the natural substrate DHFA, and that (iii) two forms of folate *viz*. folic acid and folinic acid (N5 formyl THFA) are available for therapeutic use:

(a) Which type of enzyme inhibition will be produced by Mtx?

(b) Which form of folate should be used to treat Mtx toxicity?

(see Appendix-1 for solution)

SOLUTION 4.1

SOLUTION 4.1

a. Since Mtx binds to the same site of DHFRase as the endogenous metabolite DHFA, it will act as a competitive inhibitor. However, because the binding affinity of Mtx for the enzyme is 50,000 times greater, even excess DHFA will not be able to displace it from the enzyme and nonequilibrium type of inhibition will be produced.

b. Folic acid administered as a drug will not be able to counteract Mtx toxicity because it will not be converted to the active coenzyme form THFA. On the other hand, folinic acid will supply readymade active coenzyme THFA and will be able to overcome Mtx toxicity.

PHARMACOTHERAPY, CLINICAL PHARMACOLOGY AND DRUG DEVELOPMENT

5.1 A 65-year-old male hepatic cirrhosis patient was admitted to the hospital for treatment of gross ascites. He was administered inj. furosemide 40 mg i.m. three times a day to excrete the ascitic fluid. He responded with brisk diuresis, but on the 3rd day he was found to be talking irrelevant, was weak and partly disoriented. He had a fainting episode on getting up from the bed. His serum K^+ was 2.8 mEq/L (low) and blood pH was 7.6 (raised).

(a) What is the likely cause of his condition on the 3rd day?

(b) What should be the principles of management of this complication?

(see Appendix-1 for solution)

SOLUTION 5.1

SOLUTION 5.1

a. The most likely pathogenesis of the symptoms on the 3rd day of brisk diuretic therapy in this patient is occurrence of hypokalaemic alkalosis, which precipitated hepatic encephalopathy. In cirrhotics with moderate to severe hepatic dysfunction, ammonia (NH_3) produced by gut bacteria is not completely detoxified (by conversion to urea) in the liver. Blood NH_3 tends to rise. This ionizes partly to NH_4^+ and is excreted in urine as NH_4Cl. The NH_4^+ ions do not cross the blood-brain barrier. During alkalosis, NH_3 ionizes to a lesser extent, raising blood NH_3 level which enters brain to cause encephalopathy. Weakness and postural hypotension are the other manifestations of hypokalaemic alkalosis.

b. The diuretic should be withheld till the fluid electrolyte and acid-base balance is restored. Intravenous infusion of KCl along with normal saline can hasten recovery from hypokalaemia and alkalosis. Oral lactulose (a nonabsorbable disaccharide) helps in reducing blood NH_3 level by producing acidic degradation products in the gut which convert NH_3 into poorly absorbed NH_4^+ ions. Moreover, lowering of stool pH by lactulose has a suppressant effect on NH_3 producing gut bacteria.

ADVERSE DRUG EFFECTS

6.1 A 40-year-man weighing 60 kg suffering from chronic cough with expectoration and fever was diagnosed to have cavitary pulmonary tuberculosis. He was put on the standard 1st line antitubercular regimen consisting of isoniazid (H) + rifampin (R) + pyrazinamide (Z) + ethambutol (E). His condition improved, but in the 4th week he developed jaundice with enlarged tender liver and rise in serum bilirubin as well as serum transaminase levels. He was suspected to have developed antitubercular drug induced hepatitis.

(a) Should his antitubercular treatment be stopped or continued?

(b) How would you proceed to confirm and identify the causative drug, and then select the alternative regimen?

(see Appendix-1 for solution)

SOLUTION 6.1

SOLUTION 6.1

a. The patient has a serious disease for which many effective drugs are available. As such, antitubercular treatment should be continued, albeit with nonhepatotoxic drugs.

b. The criteria for causality assessment, *viz.* temporal relationship, previous knowledge, dechallenge and rechallenge should be applied to identify the causative drug. In this case, the reaction occurred in the 4th week of drug therapy which is consistent with the time-sequencing of drug-induced hepatitis. The reaction can be confirmed and the actual causative drug identified by dechallenge and rechallenge.

- Stop all suspected drugs (H, R and Z); treat the patient with E and two other nonhepatotoxic drugs, preferably streptomycin (i.m.) and a fluoroquinolone (e.g. levofloxacin). If the jaundice clears in the subsequent weeks, dechallenge is positive (one or more of the 3 stopped drugs had caused hepatitis).
- Rechallenge by reintroducing the stopped drugs, one at a time, and repeatedly monitor liver function tests.
- Generally, R is started first followed by H after 7–10 days. If both are tolerated, Z could have been the causative drug. In any case, after completing the intensive phase with H+R+E, the continuation phase with H+R should be extended to 9 months.
- If R is implicated, it should be stopped as soon as the liver function tests become abnormal. Start H and continue H+E+S for 2 months followed by H+E for 10 months.
- If H is implicated, it should be stopped immediately, and R+E+Z may be given for 9 months.

In this way, the implicated drug can be identified and antitubercular therapy completed with minimal use of parenteral/2nd line drugs.

CHOLINERGIC SYSTEM AND DRUGS

7.1 A man aged 45 years presented with gradual onset complaints of double vision, drooping eyelids, difficulty in chewing food and weakness of limbs which is accentuated by exercise. The symptoms fluctuate in intensity over time. A provisional diagnosis of myasthenia gravis is made.

(a) Can a pharmacological test be performed to confirm/refute the diagnosis?

(b) In case the diagnosis is confirmed, can this disease be cured by medication?

(c) Is there a surgical solution for this illness?

(see Appendix-1 for solution)

SOLUTION 7.1

SOLUTION 7.1

a. The diagnosis of myasthenia gravis can be confirmed by the '*edrophonium test*'. Edrophonium is injected i.v. (2 mg initially which if tolerated; followed by 8 mg after 30–60 sec). Reversal of ptosis, diplopia and increase in the strength of affected muscles lasting 5–10 min constitutes a positive result.

   In case edrophonium is not available, the test can be performed with neostigmine 1.5 mg i.v. Atropine 0.6 mg may be given i.m./i.v. to block the muscarinic side effects of edrophonium/ neostigmine.

b. Myasthenia gravis is an autoimmune disorder due to production of antibodies against the nicotinic receptor at the muscle end-plate. No drug is curative. Both anticholinesterases (neostigmine, etc.) and corticosteroids (other immunosuppressants as well) afford only symptomatic relief till administered. The former preserve ACh and improve neuromuscular transmission, while the latter inhibit the immunological reaction, without removing the cause of the illness.

c. In many cases (especially older men), thymus is the source of the nicotinic receptor antigen. As such, thymectomy has been found to lower disease activity and even induce long-lasting remission.

ANTICHOLINERGIC DRUGS AND DRUGS ACTING ON AUTONOMIC GANGLIA

8.1 An elderly male aged 74 years was brought to the hospital since he had not passed urine for the past 24 hours and had severe pain in lower abdomen. On examination there was a bulge in the pubic region due to full urinary bladder. On catheterization, he passed 1.5L urine and the pain was relieved.

He gave the history of having difficulty in passing urine, poor stream, frequent urge to urinate and post-void dribbling for the last 3 years. Over the past few days he had been experiencing episodes of vertigo for which he was prescribed a medicine that he was taking for 2 days. Examination of the prescription revealed that he was taking tab. Dimenhydrinate 50 mg 3 times daily.

(a) Could there be any relationship between the anti-vertigo medication and the episode of acute urinary retention?

(see Appendix-1 for solution)

SOLUTION 8.1

SOLUTION 8.1

a. Dimenhydrinate is a H_1 antihistaminic-antivertigo drug with potent antimuscarinic action. Since muscarinic cholinoceptors mediate neurogenic contraction of the detrusor muscle, antimuscarinic drugs interfere with vesical contractions needed for urination. Elderly men with benign hypertrophy of prostate have bladder neck obstruction and are prone to develop urinary retention as a side effect of antimuscarinic drugs. This patient has history indicative of prostatic hypertrophy. As such, all drugs having antimuscarinic activity must be given cautiously to elderly males.

ADRENERGIC SYSTEM AND DRUGS

9.1 A lady aged 55 years presented for eye checkup. She has been having visual difficulty over the past few months, and lately she had started noticing 'halos' around the lights. She also has dull chronic ache in the forehead region. Tonometry revealed her intraocular pressure (i.o.p.) to be 22 and 24 mm Hg respectively in the left and right eye.

(a) Which mydriatic will be suitable for dilating her pupil for fundus examination and why? (see Appendix-1 for solution)

SOLUTION 9.1

SOLUTION 9.1

a. The symptoms and intraocular pressure (i.o.p.) of this patient indicate that she is having gluaucoma in both eyes. Phenylephrine (10%) eyedrop would be the suitable mydriatic for her. Phenylephrine is an α_1 adrenergic agonist that dilates the pupil by increasing the tone of radial muscles of iris, which are adrenergically innervated. It does not produce cycloplegia because the ciliary muscles lack adrenergic motor innervation. Cycloplegia causes blurring of near vision and is not required in this patient. Phenylephrine is not likely to raise i.o.p. in glaucoma patients. On the other hand, antimuscarinic mydriatics like tropicamide, cyclopentolate, etc. produce both mydriasis and cycloplegia, and tend to raise i.o.p. in glaucoma patients. Therefore, antimuscarinics are to be avoided in glaucoma patients.

ANTIADRENERGIC DRUGS AND DRUGS FOR GLAUCOMA

10.1 A 70-year-male presented with the complaints of weak stream of urine, sense of incomplete bladder voiding, urinary frequency and nocturia. After physical examination and ultrasound, he was diagnosed to have developed benign prostatic hypertrophy and was prescribed:

Tab. Terazosin 5 mg, one tab daily at bed time.

He took the medicine as advised and went off to sleep. At night, when he got up to pass urine, he felt giddy and fainted. On being laid flat on the bed, he regained consciousness within 2 minutes. Later, he was gradually propped up on the bed to the sitting position and then got up slowly and walked without any problem.

(a) What is the rationale of prescribing terazosin to this patient?

(b) What is the likely explanation for the fainting attack?

(c) What precautions could have avoided the fainting episode?

10.2 A lady aged 55 years was brought at night to the hospital emergency with severe breathlessness and wheezing. Chest auscultation revealed marked bronchoconstriction. She was managed with 100% O_2 inhalation and nebulized salbutamol + ipratropium bromide. The asthmatic attack was controlled in about 6 hours. Next day, history taking revealed that she was having mild episodic asthma off and on, but never had such a severe attack. Day before she had visited an ophthalmologist for visual difficulty and frontal headache. The intraocular pressure was measured to be 24 and 25 mmHg in right and left eye respectively. She was prescribed:

Timolol 0.5% eyedrops in each eye twice a day.

(a) What is the most likely explanation for the precipitation of severe attack of asthma?

(b) How could such a complication be avoided?

(see Appendix-1 for solutions)

SOLUTION 10.1

SOLUTION 10.1

a. The smooth muscles of the bladder neck and prostatic urethra are constricted by sympathetic innervation via α_1 adrenergic receptors. Terazosin being α_1 receptor blocker reduces the dynamic component of urinary obstruction in benign prostatic hypertrophy, improves urinary flow and affords symptomatic relief. *Contd...*

b. The α_1 adrenergic receptors also mediate reflex vasoconstriction in the lower extremity and trunk which occurs on standing up from a reclining position to maintain cerebral blood flow. Terazosin blocked these α_1 receptors as well; reflex vasoconstriction failed to occur when this patient got up from bed to pass urine; blood supply to brain suffered and the patient fainted. That is why he soon regained consciousness on being laid flat on the bed. Such an event is especially likely to occur after the first dose when compensatory haemodynamic adjustments have not taken effect.

c. The patient should have been advised not to spring up from the bed. He should first sit on the bed for few minutes and then slowly assume the erect posture. This would allow time for the reflex adjustments.

The 5 mg terazosin dose is a high starting dose. Therapy should have been initiated at 1 mg daily dose, with upward titration every 1–2 weeks according to the symptomatic relief obtained and the haemodynamic tolerance by the patient.

SOLUTION 10.2

SOLUTION 10.2

a. Timolol is a potent lipophilic, nonselective (β_1 + β_2) adrenergic blocker. In this patient of mild episodic asthma, the drug in the eyedrops appears to have been absorbed systemically during drainage through the nasolacrimal ducts and precipitated severe bronchospasm by blocking bronchodilator adrenergic β_2 receptors. Since timolol is a competitive antagonist, its action could be overcome by higher concentration of salbutamol in the nebulized aerosol supplemented with the anticholinergic ipratropium bromide to block the reflex vagal bronchoconstriction.

b. This complication could have been prevented by eliciting the history of episodic asthma and avoiding β-blocker ocular hypotensive drug. Latanoprost (a prostaglandin analogue) would be a more suitable antiglaucoma drug for this patient. In case, it was imperative to use an ocular β-blocker, the β_1 selective antagonist betaxolol would be a safer alternative. It is also prudent to start with 0.25% timolol drops and change to 0.5% drops only when needed. In any case, the patient should be advised to apply mild pressure by fingertip for few minutes at the inner canthus of the eye after each eyedrop instillation to prevent passage of the drug into the nasolacrimal duct.

HISTAMINE AND ANTIHISTAMINICS

11.1 A taxi driver aged 30 years presented with sudden onset running and itchy nose, bouts of sneezing, partial nasal blockage, redness and watering from the eyes, but no fever, bodyache or malaise. He gave history of similar episodes occurring off and on during the spring season. A diagnosis of seasonal allergic rhinitis was made and the doctor decided to prescribe antiallergic medication.

(a) Which antiallergic medicine would be suitable for this patient? Which antiallergic drugs should be avoided?

(see Appendix-1 for solution)

SOLUTION 11.1

SOLUTION 11.1

a. Since histamine is an important mediator of allergic rhinitis, the H_1 antihistaminics afford rapid symptomatic relief. A non-sedating second generation antihistaminic like loratadine, des-loratadine or fexofenadine would be suitable for this patient, who is a taxi driver. These drugs are least likely to impair alertness and driving. The first generation sedating antihistamines like promethazine, hydroxyzine, chlorpheniramine, clemastine, etc. are contraindicated if the recipient has to drive. Even the second generation antihistaminic cetirizine impairs psychomotor performance and should be avoided in this patient.

However, antihistaminics have no prophylactic effect. Because the patient has recurrent episodes during spring, he should in addition be prescribed a topical corticosteroid like budesonide or fluticasone nasal spray, starting just before and continuing all through the season to prevent further attacks of rhinitis.

PROSTAGLANDINS, LEUKOTRIENES AND PLATELET ACTIVATING FACTOR

13.1 A full term primigravida presented with labour pains. On examination the BP was 110/70 mm Hg and she was not anaemic. The presentation was vertex, head was engaged, foetal heart sound was normal, there was no cephalopelvic disproportion, no placenta previa, membranes were intact and uterine contractions were adequate. The labour was allowed to progress under observation. After 8 hours the cervix was still firm and not adequately dilated.

(a) Can some medicaion be used to soften the cervix, help its ripening and facilitate delivery? If so, which drug and route of administration should be used?

(b) Given the above findings, is there any contraindication to the use of such medication?

(see Appendix-1 for solution)

SOLUTION 13.1

SOLUTION 13.1

a. Prostaglandin E_2 (Dinoprostone) has the property to soften the cervix and make it more compliant at term. Applied to the cervix or inserted into vagina, low doses of dinoprostone act within a few hours and help to ripen the cervix so that it is 'taken up' and dilates to allow passage of the presenting part. Side effects are minimal with these routes of administration. The preferred formulation for this purpose is the cervical gel containing 0.5 mg of dinoprostone in 2.5 ml gel. It should be inserted into the cervical canal. Alternatively, the vaginal gel containing 1.0 mg in 2.5 ml should be deposited at the posterior fornix of vagina. These doses of PGE_2 only affect the cervix and do not significantly augment uterine contractions.

b. Since the patient has no anaemia or toxaemia of pregnancy or cephalopelvic disproportion, presentation is correct and head is engaged, there are no contraindications to the use of PGE_2.

NSAIDs AND ANTIPYRETIC-ANALGESICS

14.1 A 65-year-old lady presented with pain in both knees, more on the left side. The pain is worsened by walking or standing for some time. X-ray of knee shows narrowing of joint space, mild effusion and osteophytic projections. A diagnosis of osteoarthritis of knee is made. She gave history of suffering a heart attack one year back which was treated by angioplasty and a stent was placed. She regularly takes aspirin 75 mg daily for prophylaxis of further myocardial infarction.
(a) Which analgesic/NSAID will be suitable for relieving her knee pain?
(b) Which analgesic/NSAIDs should not be prescribed for her?
(c) Whether any locally applied medication can be helpful in relieving her knee pain?
(see Appendix-1 for solution)

SOLUTION 14.1

SOLUTION 14.1

a. Paracetamol taken in adequate doses (upto 2.6 g per day) is the most suitable analgesic for relieving knee pain in the given patient. Unlike many NSAIDs, it does not increase the risk of myocardial infarction/stroke. Paracetamol does not inhibit endothelial PGI_2 synthesis, does not affect platelet function and does not nullify the cardioprotective effect of low dose aspirin. Moreover, it is a first-line drug for osteoarthritic pain, and is well tolerated with minimal gastric side effects.

b. The selective COX-2 inhibitors (celecoxib, etoricoxib) are not suitable for this patient, because they increase the risk of heart attack and stroke by inhibiting endothelial PGI_2 synthesis. Diclofenac is also not free of such risk. Though propionic acid NSAIDs (ibuprofen, etc.) are nonselective COX inhibitors which do not increase thrombotic risk, they block the cardioprotective effect of low dose aspirin that this patient is taking.

c. Topical NSAIDs, e.g. diclofenac/ketoprofen gel can afford adjuvant symptomatic relief in this patient. Since blood levels of NSAIDs after local application are low, they are well tolerated and do not increase cardiovascular risk.

DRUGS FOR COUGH AND BRONCHIAL ASTHMA

16.1 A 60-year-old male patient of moderately severe chronic obstructive pulmonary disease (COPD) with FEV_1 45% of predicted, who has quit smoking for the last 5 years, and is maintained on—Ipratropium br. 20 µg/puff metered dose inhaler, 2 puffs 3 times a day, and Theophylline 400 mg SR tab. twice a day, developed sore throat and fever. He was prescribed—

Tab Erythromycin 250 mg, one tab 4 times a day for 5 days

Tab Paracetamol 500 mg 3 times a day till fever persists.

After 3 days he presented with pain in epigastrium, restlessness, irritability, inability to sleep, palpitation, tremor of fingers and hand, and had vomited twice. His fever had subsided and throat was better.

(a) What could be the reason for his recent illness?

(b) Could this illness be prevented, if so, how?

(see Appendix-1 for solution)

SOLUTION 16.1

SOLUTION 16.1

a. The recently developed symptoms of the patient are indicative of early stage theophylline toxicity. Erythromycin is an inhibitor of several hepatic microsomal enzymes, including those that metabolize theophylline. As such, when the patient took erythromycin, metabolism of theophylline appears to have been retarded, causing rise in its plasma concentration over the next 2 days and producing overdose symptoms.

b. This complication could have been prevented in *two* ways, *viz*—

   i. When erythromycin was prescribed, the daily dose of theophylline should have been reduced from 800 mg to 500 mg, and maintained at this level till the patient was taking erythromycin.

   Or

   ii. An alternative antibiotic (e.g. a β-lactam like amoxicillin or cephalexin) which does not inhibit theophylline metabolism but is effective in sore throat, could have been selected for this patient.

THYROID HORMONES AND THYROID INHIBITORS

18.1 A 20-year girl was diagnosed as a case of recent onset Graves' disease with mild diffuse pulsatile thyroid enlargement. She was treated with tab. Carbimazole 5 mg 2 tab 3 times a day. Her symptoms started subsiding after 2 weeks and were fully controlled after 3 months. The thyroid swelling also subsided and she was maintained on a dose of carbimazole 5 mg twice daily. After one year she noticed that the neck swelling was reappearing and her body weight increased by 2 kg in the last one month, but without recurrence of her earlier symptoms. She rather felt dull, sleepy and depressed. The serum TSH was 12 μU/ml and free thyroxine (FT_4) was 9 pmol/L.

(a) Why was the initial response to carbimazole delayed? Could any additional medicine be given to her initially to afford more rapid symptomatic relief?

(b) What was the cause of reappearance of the neck swelling and her condition after 1 year? What measures need to be taken at this stage?

(see Appendix-1 for solution)

SOLUTION 18.1

SOLUTION 18.1

a. Since carbimazole inhibits further synthesis of thyroid hormones (T_3, T_4) without affecting their release or action, the hormone stored in the gland continues to be released and produce effects. Moreover, thyroxine has a long plasma t½ of 6–7 days. Thus, the effect of carbimazole starts manifesting only after 2–3 weeks and peaks after 2–3 months.

   Many of the symptoms of thyrotoxicosis are due to sympathetic overactivity. Blockade of β adrenergic receptors (β_1 and β_2) by propranolol or similar drug affords rapid symptomatic relief, without affecting thyroid status. A nonselective β-blocker given to her along with carbimazole could have controlled palpitation, tremor, etc. within a few days. This drug could be withdrawn when carbimazole had taken effect.

b. The reappearance of neck swelling without any symptom of thyrotoxicosis indicates that it is due to deficient feedback inhibition of TSH by a suboptimal thyroid hormone level as a result of higher maintenance dose of carbimazole. This is supported by the mild hypothyroid symptoms experienced by the patient and the raised TSH level alongwith low normal FT_4 level. The raised TSH is stimulating the thyroid so that despite its low functional status, deficiency is not marked. Since the disease activity in Graves' disease may decline after some time, the maintenance dose of carbimazole needs to be adjusted from time-to-time according to the assessed clinical and laboratory thyroid status of the patient. This patient requires temporary discontinuation of carbimazole followed by a lower maintenance dose as assessed later.

INSULIN, ORAL HYPOGLYCAEMIC DRUGS AND GLUCAGON

19.1 During routine medical checkup a 50-year male office executive with sedentary lifestyle was diagnosed to have developed type 2 diabetes mellitus. His fasting and post-meal blood glucose was 130 mg/dl and 190 mg/dl respectively, HbA_{1c} was 7.8%, BP was 130/82 mm Hg and body mass index was 27 kg/m^2. He was asymptomatic and investigations revealed no end organ damage. He was advised suitable diet, exercise and other lifestyle modifications.

(a) Should he be prescribed an antidiabetic medication as well? If so, which drug/combination of drugs should be selected, and why?

(see Appendix-1 for solution)

SOLUTION 19.1

SOLUTION 19.1

a. According to the current recommendation of professional guidelines, the patient should be prescribed metformin therapy concurrently with dietary and lifestyle measures. This is based on the finding that metformin can delay progression of diabetes and prevent microvascular as well as macrovascular (heart attack, stroke) complications. It does not increase circulating insulin, reduces insulin resistance, is unlikely to induce hypoglycaemia and may have a positive influence on pancreatic B cell health. Lack of serious toxicity over several decades of use of metformin is well established. No other antidiabetic drug has all these favourable features, and therefore, it is considered the first-choice drug. Metformin is particularly suitable for this patient who is overweight, because it can aid weight reduction. A combination of antidiabetic drugs is not indicated at this stage. Another drug needs to be added only when the target blood glucose and HbA_{1c} levels are not attained by metformin alone.

CORTICOSTEROIDS

20.1 A 35-year female patient of inflammatory bowel disease was treated with prednisolone 40 mg/day and mesalazine 800 mg TDS. After 4 weeks, the symptoms subsided and prednisolone dose was tapered at the rate of 10 mg every 2 weeks. When she was taking 10 mg prednisolone/ day, she met with a road-side accident and suffered compound fracture of both bones of the right leg. Internal fixation of the fracture and suturing of wounds under general anaesthesia is planned.

(a) Whether any additional measure needs to be taken during surgery in view of her corticosteroid therapy?

(b) Does the prednisolone therapy need discontinuation or any alteration in the postoperative period? Give reasons.

(see Appendix-1 for solution)

SOLUTION 20.1

SOLUTION 20.1

a. The patient has received supraphysiological doses of a corticosteroid for more than 3 weeks, and is likely to have developed hypothalamo-pituitary-adrenal (HPA) suppression. The injury and surgery are a stress which need excess corticoid activity. The depressed HRA axis may not be able to cope up with increased demand, and there is risk of developing acute adrenal insufficiency. As such, hydrocortisone hemisuccinate 100 mg should be infused i.v. during surgery and repeated 8 hourly till the patient is stable.

b. Prednisolone therapy must not be stopped in the postoperative period apprehending spread of infection and delayed healing. Effective antibiotic medication to prevent wound infection should be given and prednisolone dose should be increased temporarily (for a week or so) to 20 mg/day, till the stress of the trauma and surgery subsides.

ANDROGENS AND DRUGS FOR ERECTILE DYSFUNCTION

21.1 A 65-year-old man presented with severe pain in the left shoulder region. The pain has progressively increased over the last 4 weeks, is not relieved by analgesics or NSAIDs and is worsened by pressure or movement. He also has increasing micturition difficulty for the last 6 months. Shoulder X-ray showed osteolytic lesion in the head of humerus. Rectal examination was consistent with prostate cancer which was confirmed by needle biopsy and raised serum PSA level (30 ng/ml). He refused orchidectomy and was prescribed injection triptorelin 3.75 mg i.m. to be repeated after one week and then every 4 weeks. After 1 week of 1st injection, he reported increased bone pain and greater bladder voiding difficulty. The serum PSA level was 34 ng/ml.

(a) What is the cause of the increase in bone pain and urinary obstructive symptoms? Is the choice of the drug incorrect?

(b) Could this flaring of symptoms be avoided; if so how?

(c) Can any other drug be given to relieve the bone pain?

(see Appendix-1 for solution)

SOLUTION 21.1

SOLUTION 21.1

a. This is a case of advanced metastatic prostate carcinoma, for which only palliative therapy with androgen deprivation (tumour cells remain androgen dependent) is possible. When orchidectomy has been refused, the most effective method of androgen deprivation is to give a long acting GnRH agonist. Thus, the choice of triptorelin is correct. The GnRH agonists initially increase LH (also FSH) release for 1–2 weeks, followed by receptor desensitization and nearly total blockade of LH secretion by 3–4 weeks. The raised LH levels in the beginning stimulate testis to secrete more testosterone which activates tumour cells resulting in increased bone pain and bladder obstruction noticed after 1 week of therapy in this patient.

b. The initial flaring of symptoms can be avoided by pretreating with an antiandrogen bicalutamide 50 mg orally daily for 3 days before starting triptorelin injection and then continuing both drugs together. The stimulatory effect of excess testosterone on tumour cells would be blocked by bicalutamide so that no flaring of symptoms would occur. The combined androgen blockade with GnRH agonist + androgen antagonist is the favoured approach.

c. The patient can be given an antiresorptive drug in addition to relieve bone pain. A potent parenteral bisphosphonate like zoledronate infused i.v. over 15 min every 1–4 weeks is the most effective drug for this purpose. It may also retard growth of the bony metastasis for some time.

ESTROGENS, PROGESTINS AND CONTRACEPTIVES

22.1 A 55-year-old postmenopausal woman developed a cancerous lump in the left breast for which radical mastectomy was performed. The tumour was ER positive and only one of the excised axillary lymph nodes had metastasis. She was put on adjuvant therapy with tamoxifen 20 mg per day. On her checkup visit one year later, she was found to be asymptomatic with no sign of local recurrence or lymph node enlargement, but ultrasound examination of the uterus revealed thickening of endometrium.

(a) What could be the cause and implication of the increase in endometrial thickness?

(b) Should the same adjuvant therapy continue, or should it be stopped altogether, or be replaced by another drug? Give reasons.

22.2 A 28-year-old mother with a 9 month baby wants to space out her next child and consults you for taking oral contraceptive.

(a) What questions will you ask, what physical examination will you perform and what investigations will you order before advising her whether she should take oral contraceptive or not, as well as for selecting the contraceptive preparation most suitable for her?

(see Appendix-1 for solutions)

SOLUTION 22.1

SOLUTION 22.1

a. The most likely cause of endometrial thickening in this patient is tamoxifen therapy. Tamoxifen is a selective estrogen receptor modulator (SERM) which has estrogen antagonistic action in the breast (basis of its use in breast carcinoma), but agonistic action on the endometrium which stimulates proliferation. Such unopposed (by progestin) hyperproliferation can produce thickening and predisposes to endometrial carcinoma.

b. For the reason stated above, tamoxifen should not be continued in this patient. Total stoppage of adjuvant therapy is not advisable, because estrogen suppression therapy has been shown to exert protective effect for atleast 5 years. Aromatase inhibitors, which block synthesis of estrogens in the body, have been clearly demonstrated to prevent recurrence of breast cancer, without stimulating endometrial proliferation or predisposing to endometrial carcinoma. Therefore, in this case, tamoxifen should be replaced by letrozole 2.5 mg /day or anastrozole 1.0 mg/day for the next 5 years. Due precautions to prevent osteoporosis and measures to address arthritic symptoms, if they develop, should be taken concurrently.

SOLUTION 22.2

SOLUTION 22.2

a. All diseases and conditions which contraindicate use of oral contraceptives or need caution in their use have to be ruled out before prescribing one to this subject. Full medical history, including menstrual history and past pregnancy details should be elicited. Any thromboembolic episode, jaundice or toxaemia of pregnancy should be ascertained. History of smoking, diabetes, hypertension, migraine, tuberculosis and gallbladder disease should be specifically asked. Any medication that she is taking and the reason for it should be taken into account to

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foresee possible interactions with the contraceptive. Whether she is obese or very lean also matters in selecting the contraceptive preparation. General physical examination, including palpation of breast, for any lump and a per vaginum examination for fibroid/other tumour, should be done. Blood pressure should be recorded to rule out hypertension. Fasting and postprandial blood glucose, lipid profile should be ordered to detect diabetes and dyslipidaemia. Ultrasound examination of pelvic organs should be performed for uterus size, fibroid, ovarian cyst or malignancy.

Only after all the above findings are favourable that an oral contraceptive be selected and prescribed.

OXYTOCIN AND OTHER DRUGS ACTING ON UTERUS

23.1 A full term primigravida aged 26 years is brought to the hospital with the complaint of having labour pains for the past 24 hours without making much progress. Two hours ago she had passed meconium stained liquor. The lady is in distress, mildly dehydrated and looks exhausted. The presentation is vertex and head is engaged, but cervix is incompletely dilated and uterine contractions are relatively weak. Foetal tachycardia is noted with irregularity during contractions.

(a) What course of action is appropriate?

(b) Can she be administered a uterine stimulant to strengthen the contractions? If yes, which drug should be given and how? If no, then why?

(see Appendix-1 for solution)

SOLUTION 23.1

SOLUTION 23.1

a. Though the progress of labour in this case is tardy and uterine contractions are relatively weak, there are signs of foetal distress (passage of meconium stained liquor, rapid foetal heart becoming irregular during uterine contraction). Moreover, the mother is dehydrated and exhausted. As such, the best course of action is to deliver the baby by caesarean section.
b. The mother should not be administered an oxytocic drug, because stronger uterine contractions are likely to worsen foetal distress and pose risk to the baby. The mother is also not in a fit condition to endure the stress of a difficult labour.

SKELETAL MUSCLE RELAXANTS

25.1 A 30-year lady brought to the hospital emergency with 40% burn injury has to be operated under general anaesthesia.

(a) Which muscle relaxant should be preferred for tracheal intubation and a brief surgical procedure in this patient? Give reasons.

(see Appendix-1 for solution)

SOLUTION 25.1

SOLUTION 25.1

a. Rocuronium is the preferred muscle relaxant for tracheal intubation and short lasting muscle relaxation in this patient. Succinylcholine (SCh), the fastest and shortest acting muscle relaxant which is most commonly used for aiding tracheal intubation, is not suitable for this patient, because it is a depolarizing blocker and releases K^+ from skeletal muscles. Since this patient has extensive burns and tissue injury, which itself causes hyperkalemia due to leakage of K^+ from injured cells, the K^+ released by SCh will accentuate the hyperkalemia and expose the patient to risk of cardiac arrhythmias and other complications.

Rocuronium, on the other hand, is a nondepolarizing blocker which does not trigger loss of intracellular K^+. It is the fastest acting nondepolarizing blocker with speed of action approaching that of SCh. Intubating conditions can be obtained in 60–90 sec. It also provides surgical grade relaxation for 25–40 min, along with good cardiovascular stability.

LOCAL ANAESTHETICS

26.1 A healthy full-term primigravida aged 26 years who has gone into labour presents for delivery. There is no cephalopelvic disproportion or any other contraindication to normal vaginal delivery. However, she demands relief of pain associated with labour and delivery.

(a) Can some form of regional anaesthesia be used to relieve her pain? If so, which type of regional anaesthesia with which drug would be most suitable for her?

(see Appendix-1 for solution)

SOLUTION 26.1

SOLUTION 26.1

a. Labour pain as well as that due to stretching of the birth canal can be largely relieved by spinal as well as epidural anaesthesia. It is desirable, at the same time, not to produce motor block so that the mother can actively participate in the process of labour. Since motor fibres are less sensitive to local anaesthetics (LAs) than sensory fibres, motor block of a lower level is usually produced during spinal anaesthesia. Such separation is more pronounced with epidural anaesthesia. Lidocaine and bupivacaine are the two LAs commonly used for epidural anaesthesia. Out of these, bupivacaine is more suitable for this purpose for the following reasons:

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- It provides greater separation of sensory from motor block. Separation is still larger when lower concentration (0.25% bupivacaine) is used.
- Because of higher lipid solubility, its tissue distribution is large and maternal blood levels are lower. Less drug is likely to cross to the foetus, reducing chances of neonatal depression.
- It is longer acting.

Thus, epidural anaesthesia with 0.25% bupivacaine is most suitable for this patient.

ETHYL AND METHYL ALCOHOLS

28.1 A school boy aged 16 years developed tonic-clonic epilepsy and was maintained on carbamazepine 200 mg 3 times a day. He was seizure free for the last one year, but reported back one afternoon with the complaint of recurrence of two seizure episodes since morning. On questioning, he revealed that last evening he attended a party with his friends and consumed 4 drinks of whiskey, and was awake till late night. This was the first time that he had taken an alcoholic drink.

(a) Could the recurrence of seizures be related to the intake of alcohol previous night? If so, what could be the mechanism?

(b) Does his antiepileptic therapy need any change or adjustment of doses due to this recurrence of seizures. What further advise will you give to this patient?

(see Appendix-1 for solution)

SOLUTION 28.1

SOLUTION 28.1

a. Alcohol exerts anticonvulsant action while its concentration in the brain is rising or is maintained. This is followed by lowering of seizure threshold when the concentration falls and becomes zero. Thus, recurrence of seizures in this patient could most likely be due to the temporarily increased susceptibility to seizures caused by withdrawal of alcohol from the brain.

b. Since this lowering of seizure threshold is a short-term problem, no abrupt change in antiepileptic medication or alteration of dose is warranted at this stage. The patient should be kept under observation for few days/weeks and decision about further antiepileptic therapy taken only on the basis of the subsequent course of events. The patient also must be advised to strictly avoid alcoholic drinks in future.

SEDATIVE-HYPNOTICS

29.1 A 70-year-old man consults his family physician for the problem of failing to fall asleep occasionally (3–4 times in a month) for the past few months. He usually sleeps well and has a 6–7 hour sleep duration. However, on certain nights he keeps lying in bed for 2–3 hours before getting sleep. Such episodes are unpredictable, and he cannot relate them to any disturbance, anxiety, worry or physical illness. He has tried relaxing, getting up and walking around or reading, but nothing helps. As a result, next day he feels lethargic, impaired, unable to concentrate and has poor creativity. He requests a sleeping pill that he can take after failing to fall asleep.

(a) Can he be prescribed a hypnotic for occasional use? If so, which drug would be suitable for late night intake without next morning sedation?

(see Appendix-1 for solution)

SOLUTION 29.1

SOLUTION 29.1

a. Since this patient does not require a hypnotic on regular basis, there is no identifiable cause of occasional sleep onset difficulty and he has tried non-drug measures, he can be prescribed a hypnotic to be kept handy for use when required. Because there is only sleep onset difficulty, and he will take the drug only later at night (after going to bed as usual), he needs a short acting hypnotic which would be free of residual effect next morning. Zaleplon would be suitable for this patient, as it has a short t½ (1 hour), does not cause next morning drowsiness, day time anxiety or rebound insomnia. Tolerance is unlikely to develop, because use is going to be occasional.

ANTIEPILEPTIC DRUGS

30.1 A young lady aged 25 years comes for consultation along with her husband for having suffered two episodes of fits lasting 2–3 min each over the past one week. Just before each fit, she experienced flickering in her right arm. Description of the fit given by the husband corresponds to generalized tonic-clonic seizures. She gave the history of having met a car accident about one year back in which she received head injury. There is no family history of epilepsy. General physical and neurological examination revealed no abnormality. Investigations, including EEG and MRI scan of the brain, were ordered.

(a) What instructions should be given to the husband regarding care to be taken, if and when, the next fit occurs?

(b) Should antiepileptic drug/drugs be started right away, or therapy be delayed till findings of the investigations become available or till more fits occur?

(c) In case antiseizure therapy has to be started right away, should a single drug or a combination of drugs be given? Which drug(s) would be the most appropriate for this patient?

(see Appendix-1 for solution)

SOLUTION 30.1

SOLUTION 30.1

a. The husband of the patient should be instructed that at the first sign of a seizure attack the patient should be laid on bed or ground in the prone or lateral position with neck extended to ensure free airway. A wooden/plastic gag should be placed between the teeth to prevent biting of tongue. No emergency medicine is required during or just after the fit. Only reassurance and moral support are needed. These instructions should be shared will other family members, so that anyone who is closeby may do the needful.

b. Because the patient has a history of head trauma and two seizure attacks have occurred within one week, the probability of developing epilepsy is high. As such, antiepileptic medication should be started rightaway without waiting for test reports or further fits to occur.

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c. Therapy should be initiated with a single antiepileptic drug. Antiepileptics with proven efficacy in post-head injury tonic-clonic seizures are phenobarbitone, phenytoin, carbamazepine and valproate. Since the patient is a young active lady, phenobarbitone with sedative/cognitive side effects, phenytoin with gum hyperplasia, hirsutism and other cosmetic side effects, and valproate with tremor and weight gain would be less suitable. Carbamazepine appears to be the most appropriate initial drug in this case.

ANTIPARKINSONIAN DRUGS

31.1 A 70-year-old man has been under treatment for Parkinson's disease for the last 5 years. He is currently receiving Tab. levodopa 100 mg + carbidopa 25 mg two tablets in the morning, afternoon and night. He now suffers stiffness, shaking and difficulty in getting up from bed in the morning. These symptoms decrease about ½ hour after taking the medicine, but again start worsening by noon. He notices one-sided twitching of facial muscles which is more frequent 1–2 hour after each dose of levodopa-carbidopa.

(a) Should his levodopa-carbidopa medication be stopped/replaced by another drug or the dose be increased further? Alternatively, can another drug be added to his ongoing medication? If so, should levodopa-carbidopa dose be changed or left unaltered?

(see Appendix-1 for solution)

SOLUTION 31.1

SOLUTION 31.1

a. The parkinson's disease of this patient appears to have advanced over the last 5 years and he is now experiencing 'wearing off effect' of levodopa-carbidopa. He is also developing dyskinesia, a late adverse effect of the drug. At this stage, antiparkinsonian medication cannot be withdrawn, because he will develop marked rigidity, immobility and tremor hampering life activities. He is already experiencing an adverse effect of his medication; therefore, the dose should not be increased further.

Since levodopa-carbidopa is the most efficacious and cheapest medication for parkinsonism, it may be prudent to continue it at a reduced dose and supplement it with another longer acting drug to smoothen the therapeutic effect. The options available as supplementary medication are:

- A direct dopamine agonist like ropinirole/pramipexole can be gradually added to levodopa-carbidopa whose dose should be reduced in steps. Both drugs can be taken concurrently 3 times a day. Ropinirole/pramipexole being longer acting will smoothen symptom control. They also produce less dyskinesia.
- A MAO-B inhibitor like selegiline 5 mg twice a day or rasagiline 1 mg once a day in the morning will prevent degradation of dopamine in the brain, prolonging and smoothening effect of levodopa-carbidopa.
- Entacapone 200 mg with each dose of levodopa-carbidopa can also potentiate and prolong levodopa action by inhibiting another metabolizing enzyme COMT. It can also be an additional third drug to levodopa-carbidopa + selegiline for greater symptomatic relief.

ANTIPSYCHOTIC AND ANTIMANIC DRUGS

32.1 A 25-year-male was diagnosed as a case of schizophrenia on the basis of disturbed thinking process, inappropriate talking and behaviour, restlessness, bursts of temper, anxiety, poor self-care, disturbed sleep, delusional beliefs and occasional auditory hallucinations. He was treated with tab. haloperidol 5 mg once daily at bed time. The dose was increased to 7.5 mg daily in the 2nd week and to 10 mg daily in the 3rd week. His symptoms gradually subsided and he appeared more calm and organized. However, in the 5th week his family members reported that his restlessness has reappeared, he keeps pacing around in the room, but is not aggressive or combative. On questioning the patient admited an uncontrollable urge to move around and that he feels uncomfortable in remaining still. He is not worried or anxious, but has difficulty in falling asleep.

(a) What could be the reason for the motor restlessness? Should the dose of haloperidol be increased or decreased, or should it be changed to another antipsychotic drug?

(b) Should any other drug be given to relieve the condition?

(see Appendix-1 for solution)

SOLUTION 32.1

SOLUTION 32.1

a. The most likely cause of the motor restlessness exhibited by the patient after 4 weeks of haloperidol therapy is appearance of a common extrapyramidal side effect of the antipsychotic drug called 'akathisia'. The symptom does not appear to be due to inadequate dose of haloperidol, because the psychotic symptoms have been relieved and the initial psychomotor restlessness had been controlled. There is no return of anxiety, hallucinations, etc. As such, there is no need to increase the dose of haloperidol. Dose reduction may be tried but return of psychotic symptoms is a risk. One of the atypical antipsychotic drugs may be substituted for haloperidol. Quetiapine with its sleep promoting effect will be more suitable in this case. The atypical antipsychotics have a low propensity to cause extrapyramidal motor side effects, including akathisia.

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b. For early resolution of motor restlessness, a benzodiazepine, e.g. clonazepam 1 mg or diazepam (5 mg) 2–3 times a day may be given. This may be supplemented by trihexyphenidyl 2 mg 3 times/day. In case the akathisia persists, propranolol 40 mg 2–3 times a day may be added.

ANTIDEPRESSANT AND ANTIANXIETY DRUGS

33.1 A businessman aged 35 years suffered loss and his employees left. He became very depressed and stopped taking interest in the business. Gradually he stopped going out and withdrew socially. He felt guilty, worthless and tired all the time, lost interest in pleasure and sex, stopped eating properly and had disturbed sleep. When he showed no sign of recovery even after 3 months, the family members consulted a doctor, who diagnosed him to be a case of major depression and prescribed—

Tab Sertraline 50 mg twice a day, and a multivitamin.

The family members brought him back after one week and complained that there was no improvement. On questioning the patient revealed that he felt more restless, had nausea, pain in upper abdomen, headache and no desire to eat.

(a) What could be the reason for no improvement in the depressive symptoms? Is the choice of drug inappropriate? Does the medication needs to be changed, dose increased or decreased? Should another drug be added at this stage?

(see Appendix-1 for solution)

SOLUTION 33.1

SOLUTION 33.1

a. Sertraline is a selective serotonin reuptake inhibitor (SSRI) and a first-line drug for major depression. The choice of drug is correct and the 50 mg twice daily an average dose for initiation of therapy. However, since antidepressant action of any drug (including sertraline) takes 2–4 weeks to manifest, it is too early at 1 week to expect any improvement in depressive symptoms. The dose is not subtherapeutic as indicated by appearance of mild side effects, which nevertheless are quick to appear, but to whom gradual tolerance usually develops. Restlessness, nausea, dyspepsia, epigastric distress, anorexia are expected side effects of SSRIs. The patient and his family members should be counselled to continue the medication for another 3–4 weeks by which time symptoms should start improving. The choice of drug is appropriate, and at this stage, there is no reason to change the medicine or its dose. No additional drug needs to be added at this stage.

OPIOID ANALGESICS AND ANTAGONISTS

34.1 A boy aged 14 years is brought to the hospital emergency with crush injury of both lower legs. An eye witness who brought the boy told that a bus had run over his legs about 20 min. ago. The legs were crushed but he had not bled much. He also told that initially the boy was shrieking in pain, but had fainted on way to the hospital. Preliminary examination reveals that the patient is in a semiconscious state, looks pale, the pulse is fast, low volume and collapsing. Both legs have sustained multiple fractures, the skin and soft tissues have lacerated from which blood is oozing, but there is no active bleeding. There is no apparent head injury.

(a) Should any medicine be administered immediately, before even completing a thorough physical examination? If so, which drug, by what route, and why?

(see Appendix-1 for solution)

SOLUTION 34.1

SOLUTION 34.1

a. Symptoms and signs indicate that the patient is going into neurogenic shock due to the excruciating pain of the crush injury. As such, the first priority is to relieve the acute pain. Morphine 5 mg should be injected i.v. immediately. It will not only lessen the pain and suffering of the patient, but also allay apprehension and counteract neurogenic shock. It will facilitate proper examination and first aid measures as well. Supplemental doses may be given every 2–3 hours. An i.v. infusion of saline should be started at the earliest to restore blood pressure and maintain tissue perfusion.

CNS STIMULANTS AND COGNITION ENHANCERS

35.1 A 75-year-old man was brought with a history of progressive functional decline, so much so that he now needs to be looked-after all the time. He misplaces his daily need articles, forgets what he said few minutes ago, is unable to perform simple calculations, mixes up what happened today and what happened yesterday, has poor control of emotions, but vision, hearing and other sensations are well preserved, and there is no gross ataxia. He was diagnosed to be having moderately advanced Alzheimer's disease and was prescribed Tab Donepezil 5 mg at bed time daily. After one week, his son reported that while his mental and functional state is unchanged, he has developed pain in abdomen, muscle ache, loud eructations, loose motion and is refusing to take the medicine.

(a) What could be the reason for no improvement in the mental and functional state of the patient? Are the new symptoms due to the medication? Should the drug be stopped, changed or another one added at this stage? What alternative drug could be used?

(see Appendix-1 for solution)

SOLUTION 35.1

SOLUTION 35.1

a. The primary reason for no improvement in the state of the patient is that all medicines, including donepezil, take weeks and months before any perceptible improvement in Alzheimer's symptoms become apparent. Moreover, donepezil (or any other drug) is not effective in a significant number of patients. However, one week is too short a time to know whether this patient is going to benefit or not. Since this patient has developed intolerable cholinergic side effects, they are due to donepezil which should be discontinued.

No other anticholinesterase drug is likely to be tolerated by this patient. Therefore, a drug which acts by a different mechanism could be used in this patient. Memantine is the only other drug, with documented efficacy in moderate to severe Alzheimer's disease, which is not a cholinergic drug, and which probably acts by blocking glutamate excitotoxicity. It is better tolerated and does not produce cholinergic side effects. However, improvement in memory and cognitive function is less likely, and it may only serve to slow the functional decline.

DRUGS AFFECTING RENIN-ANGIOTENSIN SYSTEM AND PLASMA KININS

36.1 A 65-year-male was diagnosed to be suffering from congestive heart failure (CHF). He had pitting edema of feet, dyspnoea and cough on mild exertion, fatigue, engorged neck veins, soft enlargement of liver, pulmonary congestion and mild cardiac dilatation. The pulse was 100/min, respiration 20/min and BP 130/86 mm of Hg. He was prescribed—

Tab furosemide 40 mg once daily in the morning

Tab captopril 25 mg twice daily, morning and evening.

After 2 hours of taking the medicines, he started passing increased quantity of urine and in the next few hours he gradually started feeling weakness, nausea, sweating and fainted while walking to the toilet. The pulse was recorded as 110/min and BP 80/40 mm Hg.

(a) What could be the cause of sudden onset symptoms and the marked fall in BP?

(b) Is the choice of drugs incorrect?

(c) How could such adverse event be prevented?

(d) What immediate management is required?

(see Appendix-1 for solution)

SOLUTION 36.1

SOLUTION 36.1

a. The weakness, nausea, sweating and fainting suffered by the patient is due to the marked rapid fall in BP caused by captopril (and augmented by furosemide). Congestive heart failure patients have an overactive renin-angiotensin system (RAS) which helps in maintaining haemodynamics in the face of low cardiac output. Captopril is a rapidly acting ACE inhibitor, which, given in doses used for hypertension, removes the RAS support (angiotensin II is not formed) and causes marked fall in BP. This is aggravated by Na^+ loss caused by the diuretic.

b. Though, a slower acting ACE inhibitor, e.g. enalapril, would be less likely to cause rapid fall in BP, captopril cannot be considered a wrong choice of drug, provided it is initiated at $1/4^{th}$ dose. In CHF, captopril therapy should be initiated at 6.25 mg dose, which can be gradually increased as haemodynamic adjustments take place.

c. The reaction could have been avoided by initiating captopril at 6.25 mg twice daily dose. A slower acting ACE inhibitor (at low starting dose) could be still less likely to produce acute hypotension.

d. The first measure to be taken in this case is to put the patient in 15° head low position. This could be supplemented by short-term fluid and electrolyte infusion. A pressor agent is rarely needed.

CARDIAC GLYCOSIDES AND DRUGS FOR HEART FAILURE

37.1 A 72-year-old man presents with swelling over ankle and feet, also noticeable over face in the morning, shortness of breath and palpitation on walking ~100 m, weakness, fatigue and cough at night. The pulse is 110/min, BP 114/78 mm Hg, there is pitting edema over feet, liver is enlarged 2 cm below costal margin, neck veins are filled upto 3 cm above clavicle, crepitations are heard at the base of lungs, apex beat is in the 6th intercostal space and heart sounds are muffled. Chest X-ray and echocardiography show enlarged cardiac shadow and an ejection fraction of 28%. A diagnosis of moderate grade congestive heart failure due to dilated cardiomyopathy is made. The doctor prescribed bed rest, salt restriction and:

Tab enalapril 5 mg twice a day

Tab furosemide 40 mg in the morning

(a) Can the patient be prescribed any other drug to hasten relief of symptoms? If so, which drug and in what dosage?

(b) Should the dose of enalapril be changed over time or should it be withdrawn, if so when?

(c) Should a β adrenergic blocking drug be added to the treatment regimen concurrently?

(see Appendix-1 for solution)

SOLUTION 37.1

SOLUTION 37.1

a. This patient of moderate CHF is in a decompensated state with dilated heart. Though, the diuretic (furosemide) and ACE inhibitor (enalapril) will relieve symptoms slowly, they may not be sufficient to restore a compensated cardiac status. Digoxin should be prescribed concurrently as it is the most effective drug for restoring compensation by increasing cardiac contractility. The features of this patient do not indicate any urgency. Therefore, the patient may be started with an average maintenance dose 0.25 mg/day of digoxin. It is expected to produce peak effect after 5–7 days. Dosage adjustment may be done after that depending on the response.

b. Enalapril dose of 5 mg twice a day should be increased by 5 mg/day at 1–2 week intervals till hypotension or other side effects appear or 40 mg/day dose is reached. For maximum prognostic benefit, ACE inhibitors have to be used at or near the highest permissible dosage. Enalapril should not be stopped unless compelled by an adverse effect, because it continues to retard worsening of CHF and avoid complications.

c. Since the patient is in a decompensated state, a β blocker cannot be added at this stage, because chances of deterioration of cardiac status are high. However, after compensation has been restored by digoxin, diuretic and enalapril and the patient is in a stable condition, a suitable β blocker may be started at a very low dose, to be upward titrated later, because β blockers afford further morbidity and mortality benefits.

ANTIARRHYTHMIC DRUGS

38.1 A sales executive aged 55 years presented with palpitation felt off-and-on, both during activity as well as at rest for the last one month or so. He also complained of tiredness and anxiety. The pulse was irregular in volume and frequency with average rate 104/min, respiration 20/min, BP 130/84 mm Hg, apex beat was irregular, with an average rate 120/min. Heart sounds were irregular, but there was no murmur. The ECG showed atrial fibrillation (AF) with no sign of ischaemia. A diagnosis of persistent AF was made, and it was decided to electrically cardiovert him. He was put on warfarin sod. 5 mg twice daily for 2 days followed by 5 mg once daily and dose to be adjusted to an INR between 2–2.5. This was to be maintained for 1 month before attempting cardioversion.

(a) Why the patient has been put on warfarin therapy before attempting cardioversion?

(b) Can some drug be given to control and regularize his heart rate in the mean time? If so, which drug(s)?

(c) If electrical cardioversion does not succeed, can some drug be given to revert him to sinus rhythm (SR)?

(d) After cardioversion, can some drug(s) be given to maintain SR and prevent recurrence of AF?

(see Appendix-1 for solution)

SOLUTION 38.1

SOLUTION 38.1

a. The patient has been having atrial fibrillation (AF) for at least the past one month. He is likely to have developed thrombii in the fibrillating atria, and is at risk of embolic stroke when sinus rhythm (SR) is restored. Therefore, he has been put on anticoagulant medication with warfarin to prevent thromboembolism. *Contd...*

b. His heart (ventricular) rate can be controlled by a drug which depresses A-V conduction. For this purpose verapamil or diltiazem or propranolol should be given orally and dose adjusted to maintain a heart rate between 60–70/min. Digoxin (0.25 mg/day) may be prescribed in addition if the target heart rate is not achieved by monotherapy.

c. If electrical cardioversion does not succeed, amiodarone 200 mg injected i.v. over 60 min may be tried for reversal to SR.

d. After restoration of SR, the same may be maintained by continued treatment with one of the following drugs, *viz.* sotalol/propafenone/amiodarone/dronedarone or disopyramide.

ANTIANGINAL AND OTHER ANTI-ISCHAEMIC DRUGS

39.1 A 55-year-old man presented with complaints of tightness and discomfort over middle part of chest felt episodically, particularly after walking briskly or climbing stairs or during sex. This is relieved within 5–10 minutes of rest. One or two episodes occur practically every day. He is a past smoker who quit smoking 5 years back when he was diagnosed to have chronic obstructive pulmonary disease (COPD), for which he regularly takes 2 inhalations of Ipratropium Br. 3 times a day and 2 puffs of salbutamol inhalation whenever he feels out of breath. The pulse was 90/min and BP 124/82 mm Hg. The resting ECG was normal, but stress test was positive. A diagnosis of exertional angina was made and he was prescribed—Tab glyceryl trinitrate 0.5 mg to be put under the tongue as soon as he begins to feel the chest discomfort, as well as before undertaking any physical exertion.

(a) Should he be prescribed another drug to be taken on a regular basis to prevent episodes of angina? If so, which drugs can be given to him and which cannot be given?

(b) Should additional medication be given to prevent long-term complications and improve survival?

(see Appendix-1 for solution)

SOLUTION 39.1

SOLUTION 39.1

a. This patient is having one or more episodes of angina practically every day; therefore, he should be prescribed regular medication to prevent the episodes. The first line drugs for this purpose which can be given to this patient are:

   1. A long-acting nitrate *viz.* oral sustained release isosorbide mononitrate or similar drug morning and afternoon or transdermal glyceryl trinitrate patch applied in the morning and taken off at night.
   2. A long-acting calcium channel blocker, like amlodipine once a day.

Alternative second line or add-on drugs are:

Nicorandil (K^+ channel opener), or ranolazine (I_{Na} current inhibitor), or trimetazidine (LC3-KAT inhibitor) or ivabradine (I_f current inhibitor).

Since he is also suffering from COPD, he cannot be given a β blocker which is likely to precipitate severe breathlessness.

b. This patient is having coronary artery disease (CAD). None of the above drugs can alter the course of CAD or prevent complications like MI or death. He should in addition be put on long-term treatment with the following to arrest/delay the progression of CAD and to afford cardioprotection:

   1. An antiplatelet drug, such as low-dose aspirin or clopidogrel.
   2. A hypolipidaemic statin, such as atorvastatin.
   3. An angiotensin converting enzyme (ACE) inhibitor, such as enalapril.

ANTIHYPERTENSIVE DRUGS

40.1 A 70-year-old male presented with complaint of dull headache, giddiness, weakness and occasional breathlessness. He gave history of left sided paralytic stroke about 2 years back, from which he has recovered nearly completely, but is taking Aspirin 75 mg per day. The pulse was 66/min. The BP was found to range between 152–160 mm Hg systolic and 82–86 mm Hg diastolic, when measured on 3 occasions over one week. The ECG showed signs of left ventricular hypertrophy, but no ischaemia. Fundus examination revealed mild age related changes. Fasting blood sugar was 96 mg/dl; kidney function, liver function tests and lipid profile were within normal range. (a) Should he be prescribed antihypertensive medication? If so, whether one, or more than one, antihypertensive should be prescribed concurrently, and which drug/drugs will be more suitable for him?

(see Appendix-1 for solution)

SOLUTION 40.1

SOLUTION 40.1

a. Since the systolic BP is above 140 mm Hg and diastolic BP is below 90 mm Hg, this patient has 'isolated systolic hypertension'. Repeated measurements have confirmed the raised BP, therefore, antihypertensive medication is indicated. Therapy should be initiated with a single drug because he is stage I hypertensive (systolic BP <160, and diastolic BP <100 mm Hg). Considering the age of the patient (>55 years), diagnosis of isolated systolic hypertension, history of stroke in the past, absence of diabetes/heart failure/ischaemic heart disease/chronic kidney disease, the most suitable antihypertensive drug for this patient is a thiazide diuretic (hydrochlorothiazide/chlorthalidone) or a long-acting dihydropyridine calcium channel blocker (like amlodipine).

Therapy may be initiated with either of these classes of drugs and later modified depending on the response and tolerability.

DIURETICS

41.1 A 50-year-old male patient of hepatic cirrhosis with ascitis and pedal edema was treated with tab Furosemide 80 mg twice a day, in addition to bed rest, suitable dietary advice and vitamin supplementation. He started passing larger quantity of urine and the ascitis/edema started regressing. After a week, he was brought with incoherent talking, drowsiness, tremor and ataxia. The relatives informed that for the past 2 days he was no longer passing the increased amount of urine as at the start of medication. Serum K^+ measurement found a value of 2.8 mEq/L.

(a) What is the cause of the neurological symptoms and diminution of the diuretic response to furosemide? Was the choice of the diuretic appropriate?

(b) How should this patient be managed at the present stage?

(see Appendix-1 for solution)

SOLUTION 41.1

SOLUTION 41.1

a. Induction of brisk diuresis with furosemide alone is not the appropriate treatment of cirrhotic edema and ascites. Hepatic cirrhosis is associated with raised aldosterone and low plasma K^+ levels. Therefore, the aldosterone antagonist spironolactone is the drug of choice. It can be supplemented by furosemide, because spironolactone alone is a weak diuretic. In this patient, use of furosemide alone resulted in further hypokalaemia and alkalosis. This indirectly raised blood NH_3 levels which crosses to the brain resulting in deterioration of mental status and neurological symptoms. Because of secondary hyperaldosteronism, the response to furosemide decreased within few days.

b. At this stage, the patient should be managed by temporarily stopping furosemide and instituting spironolactone (50 mg 6 hourly) therapy along with appropriate i.v. fluid and electrolyte infusion to correct the imbalance, guided by repeated plasma level monitoring. After restoration of the fluid/electrolyte balance and his mental status, the patient should be put on maintenance therapy with spironolactone (100–400 mg/day) and furosemide (40–160 mg/day) with dose adjustment according to response. If hormonal side effects of spironolactone occur, it may be substituted by the other aldosterone antagonist eplerenone. The potassium sparing non-aldosterone antagonist diuretic amiloride is an alternative.

HAEMATINICS AND ERYTHROPOIETIN

43.1 A lady aged 40 years consults you for treatment of her anaemia that is not improving with medicine prescribed by a local doctor. She told that she is suffering from weakness, fatigue and occasional giddiness for the last 4–5 months. She went to a local doctor 2 months ago who got her blood tested, which showed Hb was 7.5 g/dl. A liquid medicine was prescribed, that she has been taking 1 tablespoonful daily without any benefit. The medicine was found to be syrup Ferric ammonium citrate 160 mg/15 ml along with folic acid 0.5 mg and vit B_{12} 7.5 µg. She also revealed that she suffers from heart burn, and has been taking a tablet (Rabeprazole 20 mg) once daily for the last 2–3 years. Repeat blood testing showed Hb to be 7.6 g/dl, haematocrit was 27%, RBCs were microcytic-hypochromic, and other values were consistent with iron deficiency anaemia. Her periods were normal and detailed examination showed no evidence of bleeding from any site.

(a) What could be the reason for her failure to improve with oral iron therapy that she has been taking?

(b) Can she still be treated with oral iron, or does she require parenteral iron therapy? What treatment would be appropriate for her?

(see Appendix-1 for solution)

SOLUTION 43.1

SOLUTION 43.1

a. There are several reasons which could account for failure of this patient of iron deficiency anaemia to respond to the oral iron medication she has been taking:
   - Taking 160 mg of ferric ammonium citrate (iron content 20%) would provide just 32 mg of elemental iron/day. This is grossly inadequate to treat iron deficiency, for which 200 mg of elemental iron/day is required to yield optimum response.
   - Iron in ferric ammonium citrate needs to be reduced to ferrous form before absorption. Therefore, its bioavailability is lower compared to ferrous salts.
   - Gastric acid is required to reduce ferric iron to ferrous iron and to facilitate iron absorption. This patient is taking acid suppressant medication (rabeprazole, a proton pump inhibitor).

   As such absorption of iron from the medicine that she took could be very low.

b. Since there are obvious factors in this case which can be tackled, it would be inappropriate to abandon oral iron therapy at this stage and jump on to injectable iron. Proper selection of oral iron preparation and its dose, and careful management of therapy may yield a response in this patient. A ferrous salt with high iron content like ferrous sulphate or ferrous fumarate (both having ~33% iron) should be prescribed in a dose of 200 mg 3 times a day (total 600 mg or 200 mg elemental iron/day). However, therapy should be initiated with a low dose to be gradually increased as the gastrointestinal tract adjusts to the medication and tolerance to side effects develops. The doses should preferably be taken in empty stomach, but if gastric discomfort occurs, it may be given with food. Selection of ferrous salt would reduce dependence on gastric acid for absorption of iron. However, if tolerated, an effort should be made to discontinue rabeprazole.

DRUGS AFFECTING COAGULATION, BLEEDING AND THROMBOSIS

44.1 A 35-year-old woman was on maintenance therapy with warfarin for leg vein thrombosis that she had developed during a complicated delivery 2 months back. The dose was adjusted by repeated measurement of INR, and for the last one month it was maintained between 2.4–2.8 with 4 mg taken daily at bed time. She developed a pelvic infection for which she was admitted to the hospital and given Inj. Ceftriaxone 1 g i.v. 8 hourly. On the 3rd day she started bleeding per-vaginum and reported passing dark urine. The haemoglobin level fell to 9.0 g/dl, while on admission 3 days back, it was 11.0 g/dl. The INR was measured to be 5.4.

(a) What could be the cause of bleeding per-vaginum, passing dark urine; fall in Hb level and rise in INR value? Could this complication be prevented?

(b) How should this patient be managed?

(see Appendix-1 for solution)

SOLUTION 44.1

SOLUTION 44.1

a. Passage of dark urine indicates bleeding in the kidney. This along with blood loss per vaginum has resulted in acute fall in Hb level. The rise in INR value is indicative of excessive deficiency of clotting factors, especially of prothrombin, factor X and factor VII due to relative warfarin overdose. The obvious cause in this patient is the additive hypoprothrombinaemic action of inj ceftriaxone given for treatment of pelvic infection.

   This complication could have been prevented either by selecting an antibiotic that does not cause hypoprothrombinaemia/interact with warfarin or by reducing the dose of warfarin when ceftriaxone was started. The new warfarin dose should have been arrived at by repeated determination of INR value till ceftriaxone was being given.

b. Further warfarin dose must be stopped immediately and vit K 10 mg injected i.m. at the earliest. The patient must be put on bed rest to reduce bleeding. Because Hb level is 9 g/dl, blood transfusion is not required at this stage, but must be kept handy in case she bleeds further. Repeat doses of vit K (5.0 mg i.m.) should be guided by frequent INR measurement and the severity of bleeding, avoiding too much vit K that would interfere with the protective effect of warfarin subsequently. Changing the antibiotic to one which does not cause hypoprothrombinaemia or bleeding may be considered on the basis of bacteriological sensitivity of the organism causing pelvic infection.

HYPOLIPIDAEMIC DRUGS AND PLASMA EXPANDERS

45.1 The routine medical checkup of a 50-year-old male, asymptomatic, non-smoker business executive with sendentary job and no family history of premature cardiac death has yielded the following findings:

Body mass index—27, waist circumferance—92 cm (38"), BP—130/86 mm Hg, fasting blood glucose—98 mg/dl, total serum cholesterol (CH) 268 mg/dl, LDL-CH 198 mg/dl, HDL-CH 38 mg/dl, serum triglyceride 160 mg/dl. Liver, kidney and thyroid function test values and ECG are within normal limits. There are no remarkable findings on physical examination.

(a) Apart from counselling on life-style modification, does this person require any medication?

(b) In case he needs medication, which drug and dose would be appropriate? What should be the goal of drug therapy?

(see Appendix-1 for solution)

SOLUTION 45.1

SOLUTION 45.1

a. This subject, though asymptomatic, has four risk factors for coronary artery disease (CAD), *viz*.

   (i) He is a male above 45-year age, (ii) his body mass index (BMI) is >25, (iii) total and LDL-cholesterol (CH) are raised to values that are above the threshold for initiation of hypolipidaemic drug therapy, (iv) the HDL-CH is low (<40 mg/dl). Thus, apart from life-style changes to regulate diet, reduce body weight and increase physical exercise, he requires lipid lowering medication.

b. In view of his lipid profile, he should be treated with a 'statin' drug to lower LDL-CH to below 130 mg/dl. Thus, a 40% reduction in LDL-CH should be aimed. This is likely to be achieved by atorvastatin 20 mg/day or simvastatin 40 mg/day. After treating with either of the above medication for 4–6 weeks, attainment of the goal LDL-CH (<130 mg/dl) should be checked. In case, it is not met, the dose may be doubled. The aim should be to maintain his LDL-CH below 130 mg/dl. With this therapy, the TG level, which is borderline, is also expected to decrease and HDL-CH level to rise above 40 mg/dl.

DRUGS FOR PEPTIC ULCER AND G.E.R.D.

46.1 A 45-year-old male patient presents with dyspepsia and dull epigastric pain which has been worsening gradually over the last one month. The pain is partly relieved by food, but becomes worse after 2 hours or so. Heart burn and pain which awakens him is often felt at night. Epigastric tenderness is detected on palpation. Upper gastrointestinal endoscopy reveals an ulcer measuring 12 mm X 18 mm in the 1st part of duodenum. His medical records show that he suffered similar episode of pain about 9 months ago. No endoscopy was done, but he was treated with omeprazole 20 mg OD for 6 weeks. Subsequently, nearly 3 months back, he suffered from loose motions and abdominal pain which was treated with a 5 day course of metronidazole + norfloxacin. Facility for *H. pylori* testing is not available. There is no history of NSAID use.

(a) What would be the most appropriate treatment option for him to achieve fast symptom relief, ulcer healing and prevention of further recurrences?

(see Appendix-1 for solution)

SOLUTION 46.1

SOLUTION 46.1

a. This patient is suffering from recurrent peptic ulcer disease. The earlier episode of similar symptoms had responded to proton pump inhibitor (PPI) therapy. Therefore, it was also due to peptic ulcer. Symptom relief and ulcer healing can be achieved this time as well with the use of a PPI given for 4–8 weeks depending on endoscopic confirmation of ulcer healing. However, it alone cannot prevent recurrences, which most commonly are caused by persistent

Contd...

colonization of upper gastrointestinal tract by *H. pylori*. Since the same cannot be confirmed in the absence of testing facility, he should be given the benefit of *H. pylori* eradication therapy which largely prevents ulcer recurrences. A 3 drug, 2 week regimen would be the most effective option. Since he has a history of metronidazole use in the recent past, chances of nitroimidazole resistance are high, and he should be treated with a PPI (omeprazole 20 mg/lansoprazole 30 mg/pantoprazole 40 mg/rabeprazole 20 mg) + amoxicillin 750 mg + clarithromycin 500 mg, all given twice daily. The PPI should then be continued till endoscopic confirmation of healing is obtained, because the ulcer was larger than 10 mm in diameter.

ANTIEMETIC, PROKINETIC AND DIGESTANT DRUGS

47.1 A 4-year-old girl is brought to the hospital emergency. The parents are very alarmed by her condition that has developed over the past one hour, when she started making bizarre faces. The neck has become rigid and head has tilted to one side. The teeth are clinched and she is not speaking. The eyes are staring in one direction and there are intermittent purposeless movements of the upper limbs. The parents inform that she had vomited twice in the morning and was taken to a local doctor, who had given her an injection. The vomiting had stopped, but after about 2 hours of the injection she developed the above symptoms.

(a) What is the most likely cause of her symptoms? Could it be due to the injection given to her? If so, which drug could have caused it?

(b) How should this patient be treated?

(see Appendix-1 for solution)

SOLUTION 47.1

SOLUTION 47.1

a. This child has developed acute muscular dystonia, an extrapyramidal motor reaction that can be caused by drugs with dopaminergic D2 receptor blocking action. Antiemetics with D2 blocking action are chlorpromazine and related neuroleptics like trifluprom azine, prochlorperazine, etc. and prokinetic drug metoclopramide. It is likely that the girl was given injection of one of these drugs by the local doctor, following which the vomiting had subsided and the dystonia had developed within 2–3 hours.

b. Though the dystonic reaction usually passes off within a few hours, it can be rapidly reversed by a parenterally administered centrally acting anticholinergic drug. Since the parents are alarmed and to afford quick relief, she may be given a deep intramuscular injection of 10–15 mg of promethazine or hydroxyzine, which have anticholinergic, antihistaminergic, sedative and antiemetic properties. This can reverse the dystonia within 15–30 min.

DRUGS FOR CONSTIPATION AND DIARRHOEA

48.1 A 35-year-old man has come with complaint of acute onset diarrhoea. The stools are relatively small volume, liquid but not watery, frothy and are preceded by griping pain in abdomen. Foul smelling wind, eructation and mild fever are the other complaints. He has passed 4 loose motions in the past 8 hours and there is no appetite. He admits to have eaten spicy snacks last evening at a road side stall. Physical examination reveals body temperature 101°F, no signs of dehydration, but diffuse abdominal tenderness. A tentative diagnosis of enteroinvasive diarrhoea is made.

(a) Does this patient require rehydration therapy?

(b) Should an antibiotic be prescribed? If so, which antibiotic would be appropriate?

(c) Should an antimotility-antidiarrhoeal drug be coprescribed to reduce the number of stools?

(d) Should any other symptomatic drug be given to him?

(see Appendix-1 for solution)

SOLUTION 48.1

SOLUTION 48.1

a. This patient of diarrhoea seems to have lost only small amount of fluid and there are no signs of dehydration. Moreover, he is a young adult. Thus, there is no need of rehydration therapy, but normal fluid intake and nutrition should be continued.

b. The features of this patient including fever are indicative of moderately severe enteroinvasive infection. As such, antibiotic therapy is indicated. A well absorbed fluoroquinolone like ciprofloxacin or ofloxacin would be suitable first line antibiotic for empiric therapy.

c. Antimotility-antidiarrhoeal drug is contraindicated in this patient, because in all likelyhood there is enteroinvasive infection, so that restriction of bowel clearance can favour further bowel wall invasion and systemic spread of the pathogen.

d. Symptomatic relief of fever can be afforded by paracetamol 500 mg 6 hourly. Abdominal pain can be dampened by an antispasmodic drug like dicyclomine 20 mg 6–8 hourly.

ANTIMICROBIAL DRUGS- GENERAL CONSIDERATIONS

49.1 A lady aged 40 years and weighing 60 kg is to undergo elective cholecystectomy for multiple gallstones. She is asymptomatic.

(a) Does she require antimicrobial prophylaxis?

(b) If she does, which antimicrobial(s) should be selected? When, by what route and dose, and how long the antimicrobial(s) should be administered?

(see Appendix-1 for solution)

SOLUTION 49.1

SOLUTION 49.1

a. Since this is an elective surgery with no indication of any infection in the operative area, but where the biliary tract is going to be cut, with no/minimal spillage or contact with infected material expected, it may be categorized as 'clean-contaminated' surgery. As such, she requires to be given antimicrobial prophylaxis.

Contd...

b. The surgery involves cutting the biliary tract. Therefore, prophylaxis covering aerobic as well as anaerobic organisms and both gram-negative as well as gram-positive bacteria would be appropriate. Drugs recommended are:

	Cefuroxime	1.5 g i.v.	+ metronidazole 0.5 g i.v.
or	gentamicin	160 mg i.v.	

Single dose injected i.v. within 30 min before surgery. Normally, there is no need to repeat the injection, but if the surgery lasts more than 2 hours, a repeat injection after surgery may be given.

SULFONAMIDES, COTRIMOXAZOLE AND QUINOLONES

50.1 A 62-year-old lady presented with acute onset frontal headache which is worse in the morning, thick, yellowish discharge from the nose, nasal blockage and fever for the past 2 days. She has been suffering from cold and cough for the last one week. The forehead is tender on pressing, particularly in the middle. A plain X-ray of the face and head showed both sided frontal sinusitis. Her husband informed that 3 months back she sufferred an episode of depression, for which she is receiving Tab amitryptyline 75 mg once daily at bed time and her mental condition is stable now. The doctor decides to start empirical therapy with moxifloxacin 400 mg once daily for 10 days. He also prescribes paracetamol 500 mg 8 hourly for fever and oxymetazoline nasal drops twice daily for blocked nose.

(a) Is the choice of antibiotic appropriate for her? If yes, what could be the considerations for selecting moxifloxacin. If no, then give reasons, and suggest the alternative antibiotic(s) that would be appropriate.

(see Appendix-1 for solution)

SOLUTION 50.1

SOLUTION 50.1

a. Moxifloxacin is a 2nd generation fluoroquinolone (FQ) antibiotic with high activity against gram positive cocci which are primarily involved in acute sinusitis. Moreover, it has a convenient once a day oral dosing schedule and is generally well tolerated. It has been used in sinusitis with high success rates. These could be the considerations on the basis of which the doctor has decided to use moxifloxacin. However, moxifloxacin is *not* appropirate for this patient because she is receiving amitryptyline, a tricyclic antidepressant which has proarrhythmic potential. Moxifloxacin can prolong Q-T interval and increase the risk of serious cardiac arrhythmias such as *Torsades de pointes* when given along with amitryptyline.

Other antibiotics which are active against gram-positive cocci and suitable for treating sinusitis are amoxicillin alone or with clavulanic acid, a first generation cephalosporin or azithromycin. These antibiotics donot carry the risk of precipitating arrhythmias.

BETA-LACTAM ANTIBIOTICS

51.1 A 10-year-old boy weighing 25 kg is brought with continuous fever for the past 7 days. Initially the fever was mild, but has gradually increased and the body temp. now is 103°F. The boy also complains of abdominal pain, bloating, loose motions, loss of appetite, occasional vomiting, weakness, malaise and cough. A local doctor had given some tablets for the past 3 days, but the condition has worsened. He looks ill, mildly dehydrated with coated tongue; pulse is 70/min, abdomen is distended and tender on pressing. Liver and spleen are palpable. The total leucocyte count is 5000/cumm. Blood for culture is sent. A provisional diagnosis of *typhoid (enteric)* fever is made.

(a) Should antibiotic therapy be started right away, or the report of blood culture awaited?

(b) If treatment is to be started, which antibiotic would be the most appropriate, and why? What should be the dose and duration of antibiotic therapy?

(c) Should a single antibiotic or a combination be used?

(*see* Appendix-1 for solution)

SOLUTION 51.1

SOLUTION 51.1

a. In this patient antibiotic therapy should be started on the basis of clinical diagnosis, because the patient is quite sick. Rapid relief of symptoms and cure should be the aim. Moreover, blood culture is not necessarily positive in all cases of typhoid fever. Treatment cannot be withheld for want of confirmation by culture.

b. The most appropriate antibiotic is ceftriaxone (or a similar 3rd generation cephalosporin like cefoperazone, cefotaxime), becuase it produces the fastest and surest response. Moreover, being bactericidal it prevents relapse and the risk of carrier state. Being long acting, ceftriaxone can be given as a once daily injection. The daily dose for this boy would be (75 mg/kg x 25 kg) = 1875 mg or rounded off to 2.0 g per day, given as slow i.v. injection once daily. The dose may be halved after 2 days or when fever subsides. It should be given till 2 days after the fever subsides totally.

c. In case of typhoid fever, a single antibiotic is sufficient, since addition of another antibiotic has not been found to hasten or improve the response.

TETRACYCLINES AND CHLORAMPHENICOL

52.1 A 30-year-old mother of 2 children attends the gynaecology OPD of the District Hospital with the complaint of whitish watery foul smelling vaginal discharge for the past 2 months. She also suffers lower backache and feels deep pelvic pain during intercourse, which she has irregularly, because her husband works in the city and visits her off and on. She feels weak, but there is no fever. Her periods are regular, but somewhat painful. Last menstruation was 10 days back. Vaginal examination reveals mucopurulent discharge from the cervical canal and pelvic tenderness, but there is no pelvic mass or abscess. She expresses inability to get any investigations done, as she is poor and has to return to her village. A provisional diagnosis of chlamydial nonspecific endocervicitis is made, with possibility of gonococcal infection, concurrently or alone.

(a) What is the most appropriate drug treatment for her?

(b) Should her husband be also examined and treated?

(see Appendix-1 for solution)

SOLUTION 52.1

SOLUTION 52.1

a. The most appropriate drugs and regimens for treating chlamydial endocervicitis are: Azithromycin 1.0 g (2 tabs of 500 mg) single dose, or Doxycycline 100 mg twice daily for 7 days. Both these regimens are adequate to treat uncomplicated gonococcal infection as well as concurrent chlamydial and gonococcal infection. Both these antibiotics are oral and well tolerated. While azithromycin has the advantage of single dose treatment, doxycycline needs twice daily dosing for one week, but is cheaper.

   Other first choice antibiotics like amoxicillin and ceftriaxone for gonorrhoea are not effective against chlamydia.

b. Both these infections are sexually transmitted diseases. Her husband is also likely to be infected. She must be counselled to get her husband examined and treated concurrently.

AMINOGLYCOSIDE ANTIBIOTICS

53.1 A 75-year-old unconscious male patient of cerebral stroke is maintained on ventilator in the intensive care unit of the hospital. On the 4th day he developed fever, and the total leucocyte count rose to 14000/µL, along with signs of chest infection. A sample of bronchial aspirate is sent for bacteriological tests, and it is decided to institute empirical treatment with cefotaxime and gentamicin. His body weight is 60 kg and creatinine clearance is estimated to be 50 ml/min.

(a) What should be the appropriate dose and dosing regimen for gentamicin and cefotaxime for this patient?

(see Appendix-1 for solution)

SOLUTION 53.1

SOLUTION 53.1

a. The recommended dose range of gentamicin for a person with normal renal function is 3–5 mg/kg/day (or 4 mg/kg/day on average). For a patient with creatinine clearance value of 50 ml/min, the dose has to be reduced to 50%, or 2 mg/kg/day. In this patient weighing 60 kg, it would be 120 mg/day. With renal impairment, this patient is not suitable for once daily dosing regimen, and he should be treated with the conventional 8 hourly regimen. As such, he may be injected with gentamicin 40 mg every 8 hours making it 120 mg/24 hours. Since the patient is unconscious and in ICU, an i.v. line must have been maintained. Gentamicin may be injected through the i.v. line taking 30 min to complete the injection. Alternatively, it may be injected i.m.

The usual dose-range of cefotaxime for an adult is 1–2 g every 6–12 hours (2–8 g/day). This patient has renal impairment, half life of cefotaxime is likely to be prolonged. Therefore, a dose near the lower end the range would be appropriate for him. As such, a dose of 1 g every 8 hours (3 g/day) may be selected. This may be slowly injected in the i.v. line or given by i.m. route.

MACROLIDE AND OTHER ANTIBACTERIAL ANTIBIOTICS

54.1 A 35-year-old woman came to the OPD with complaints of urinary urgency, pain and burning during urination, suprapubic discomfort and low-grade fluctuating fever for the past 2 days. She had 3–4 similar episodes over the last year, for which she took treatment from a local doctor. She is married, has 3 children and her last menstrual period was 10 days back. She is neither using nor is willing to use a contraceptive. Physical examination reveals tenderness in the suprapubic region and body temperature 100.4°F. A diagnosis of acute cystitis is made and she is advised to get urine culture and blood tests done.

(a) Should empirical antimicrobial treatment be started after urine sample has been taken for testing? If so, which drug(s) would be appropriate?

(b) Can any drug be given to rapidly relieve urinary symptoms?

(c) Should long-term prophylactic drug be prescribed in her case? If so, which drug would be suitable for her?

(see Appendix-1 for solution)

SOLUTION 54.1

SOLUTION 54.1

a. Since the patient has distressing urinary symptoms and is febrile, empirical antimicrobial treatment should be started after urine has been collected for bacteriological testing. Moreover, in a sexually active woman, lower urinary tract infections (UTI) are moslty treated empirically. The first line antimicrobials for this purpose are fluoroquinolones, cotrimoxazole, amoxicillin-clavulanate, an oral 1st or 2nd generation cephalosporin, or nitrofurantoin. Any of these may be selected and prescribed for 3–5 days depending on symptom resolution. She should be avised to abstain from sexual intercouse in this period. Nitrofurantoin is usually not preferred because it needs at least 7 days treatment, and often causes nausea and gastric pain.

b. Phenazopyridine is a urinary analgesic with no antimicrobial activity. It relieves symptoms of bladder and uretheral irritation and can be given with the selected antimicrobial drug.

c. Because this patient has suffered >3 episodes of cystitis within one year, she should be advised long term prophylactic therapy. The suitable prophylactic drug for her is cephalexin 250 mg once daily at bed time, because it is not contraindicated in pregnant women. Though this patient is not presently pregnant, she may conceive during use of the prophylactic drug. The other recommended prophylactic drugs, *viz* cotrimoxazole, nitrofurantoin and norfloxacin are all contraindicated during pregnancy.

ANTITUBERCULAR DRUGS

55.1 A 45-year-old male factory worker weighing 60 kg reports to the hospital with cough and expectoration, mild chest pain, weakness and fatigue for the last one month. In addition he has developed low grade fever for the last one week. He gives history of having suffered from TB of the lung one year back for which he took treatment from the hospital and became all right in 2 months. He stopped taking the medicines after another 1 month, though he was told by the doctor to continue treatment. The sputum was found to be positive for AFB and X-ray chest showed a 5 cm cavitary lesion in the right middle lobe and fibrotic changes in the upper lobe. He was diagnosed to be a defaulted patient of pulmonary TB.

(a) Should any specific laboratory test be ordered in this case; if so, should the treatment start immediately or after the report is available?

(b) What should be the regimen of antitubercular drugs for this patient? Can he be treated with a thrice weekly dosing regimen?

(*see* Appendix-1 for solution)

SOLUTION 55.1

SOLUTION 55.1

a. Since the patient is a previously treated case of TB, it is important to find out the drug resistance status of the bacilli infecting him. Sputum culture for AFB and sensitivity testing should be ordered. However, chemotherapy should be started immediately, because the culture and sensitivity tests take 6 weeks or more and defering treatment for such a long time may jeopardise outcome.

b. Selecting the anti-TB regimen for retreatment patients is guided by assessment of risk of multidrug resistance (MDR) TB. This is a defaulted patient who has taken isoniazid and rifampin only for 3 months. As such, risk of MDR-TB may be categorized as low and he should be treated with the 8 month regimen of 1st line drugs. For the initial 2 months, he should be given all 5 first line drugs, *viz* isoniazid 300 mg + rifampin 600 mg + pyrazinamide 1.5 g + ethambutol 1.0 g all orally and streptomycin 1.0 g i.m. daily. Streptomycin should be stopped after that and the 4 oral drugs given for another 1 month. Pyrazinamide should be discontinued and 3 drugs rifampin, isoniazid and ethambutol should be continued for 5 more months. This is a retreatment case, who should be given drugs daily under supervision. The thrice weekly regimen carries higher risk of drug resistance in his case. The regimen may be modified when the culture and sensitivity report becomes available.

ANTILEPROTIC DRUGS

56.1 A 50-year-old male attends the hospital OPD with multiple, diffusely raised nodules over the face and arms for the past 1 month. The skin over the lesions is reddish and glossy. Sensation over face and arms is diminished and the ulnar nerve is thickened. He informs that 6 years back he had suffered from similar lesions and had taken regular medication for the same for one year and was declared cured. The treatment records revealed that he was given the standard multidrug therapy with rifampin, clofazimine and dapsone and had successfully completed the one year course. The skin smear is positive for *M. leprae*.

(a) What could be the cause of relapse of leprosy in this case? What treatment should be prescribed?

(*see* Appendix-1 for solution)

SOLUTION 56.1

SOLUTION 56.1

a. Since the patient had taken the standard multidrug therapy for the prescribed one year, and had responded clinically, the most likely cause of relapse is reactivation of dormant (persister) bacilli. Development of resistance to the multidrug regimen is very rare. The reactivated persisters remain sensitive to the same drugs. As such, he should be treated with the same drugs, *viz* rifampin 600 mg + clofazimine 300 mg once a month alongwith dapsone 100 mg + clofazimine 50 mg daily for one year.

ANTIFUNGAL DRUGS

57.1 A 50-year-old woman presents with complaints of constant pain in the retrosternal region for the past 2 weeks. The pain is markedly aggravated during swallowing. The condition has progressively worsened, and now even drinking water hurts. There is difficulty in swallowing as well. She informs that she is a diabetic and takes Tab. Glibenclamide 5 mg twice a day for the past two years, but has not checked her blood glucose for the last few months. Endoscopy reveals diffuse streaks of creamy yellow mucosal plaques and a few erosions in the esophagus. Scrapings from the plaque are sent for microbiological examination. Fasting blood glucose is found to be 180 mg/dl. She is diagnosed as a case of esophageal candidiasis with poorly controlled diabetes mellitus.

(a) What drug/drugs should be prescribed to treat her esophageal condition? What should be the duration of therapy?

(b) What are the aspects to be considered in view of the fact that the patient is a poorly controlled diabetic taking a sulfonylurea medication?

(*see* Appendix-1 for solution)

SOLUTION 57.1

SOLUTION 57.1

a. The treatment of choice for *Candida* esophagitis is oral fluconazole 100 mg/day for 3 weeks, because it is highly effective and well tolerated. However, some cases do not respond due to fluconazole resistance. These may be treated with itraconazole 200/day or voriconazole 200 mg twice daily.

b. Uncontrolled diabetes is an important predisposing factor in the causation of esophageal candidiasis, and appears to have played a role in this patient. Therefore, measures to achieve quick glycaemia control are needed. Since the patient already had a complication of diabetes (*Candida* infection) it is desirable to shift her to insulin therapy (at least till the esophagitis is fully cured). The dose and frequency of insulin injections should be guided by repeated blood glucose monitoring. Fluconazole (other azoles as well) inhibit CYP450 isoenzymes and raise the blood levels of salfonylureas. The intensity of action of glibenclamide (if continued in this case) is likely to be affected unpredictably. Thus, even if this drug is continued, close monitoring of blood glucose level and dose adjustment of the sulfonylurea is required.

ANTIVIRAL DRUGS

58.1 A dental surgeon consults you with the following problem:

During a dental procedure he got exposed to a 26-year-old female patient's blood and saliva through a piercing injury on the finger. A needle had penetrated across his gloves and skin to a depth of 2–3 mm, but was withdrawn immediately and the area washed under running water. On enquiry, the patient revealed that one year back she had tested HIV positive, but was asymptomatic and not taking any anti-HIV medication.

(a) Should the dental surgeon be advised to take post-exposure prophylactic medication for HIV, or no medication is indicated under the circumstances?

(b) If medication is advised, which drug/drugs, doses and duration of use would be appropriate?

(*see* Appendix-1 for solution)

SOLUTION 58.1

SOLUTION 58.1

a. Considering the facts of injury and exposure in this case, the risk of contacting HIV infection by the dental surgeon is very low. However, HIV disease can only be prevented, but not cured, and has serious implications. Moreover, even a few virions entering the body can set up an infection. Therefore, it would be prudent to give prophylactic medication to further cut down chances of acquiring the infection.

b. Because the given case is of the low risk category, and the source person is neither symptomatic nor taking any anti-HIV medication, the standard 2 drug prophylaxis would be appropriate. The dental surgeon should be advised to immediately start taking—
Zidovudine 300 mg + Lamivudine 150 mg twice daily for 4 weeks.

ANTIMALARIAL DRUGS

59.1 A 20-year-old girl reported to the district hospital OPD with irregular episodes of high fever for the past 3 days. The fever is preceded by chills and shivering and attended by headache, body ache, pain in abdomen, nausea and weakness. The fever lasts 4–6 hours and subsides after sweating. On enquiry she informed that she belongs to a village in the tribal area of Madhya Pradesh. About a month back she had returned from her home after a 3 weeks vacation and she works as a house maid in the city. Blood smear examination showed presence of intraerythrocytic *P. vivax* parasites. She was treated with the standard 1.5 g chloroquine (base) course over 3 days, and was given primaquine 15 mg tab to be taken once daily for 14 days, after she tested negative for G-6PD deficiency. She was afebrile on the 4^{th} day, but returned back 7 days later with similar episode of chills and fever. Finger prick blood smear was positive for *P. vivax*. She confirmed continuing to take daily primaquine medication.

(a) What is the most likely cause of recurrence of fever and parasitaemia?

(b) How should the 2^{nd} episode of fever be treated?

(c) Should primaquine medication be continued or stopped?

(*see* Appendix-1 for solution)

SOLUTION 59.1

SOLUTION 59.1

a. Recurrence of fever after being afebrile for 7 days indicates 'recrudescence' due to incomplete parasitaemia clearance by the treatment given for the 1st episode of fever. This occurs due to low grade chloroquine-resistance. While majority of asexual schizonts are killed by chloroquine and the fever subsides, some survive and multiply to cause fever again. The second episode of fever is not due to 'relapse' which is caused by *vivax* hypnozoites reinvading RBCs. Relapse generally occurs after 3 weeks to few months. Moreover, the patient is taking primaquine which kills hypnozoites.

b. As broughtout above, recrudescence indicates chloroquine-resistance, which is particularly likely in this case, because the infection appears to be contacted from an area where chloroquine-resistance among *P. vivax* has been detected. As such, she should be treated with an alternative drug effective against chloroquine-resistant *P. vivax*. These are:
   1. Quinine 600 mg three times a day for 7 days along with doxycycline 100 mg once daily for 7 days.
   2. Artesunate 100 mg twice daily for 3 days, along with a single dose of sulfadoxine 1500 mg + pyrimethamine 75 mg.

c. The primaquine therapy should be continued to complete the 14-day course, so as to totally eradicate the *P. vivax* hypnozoites from the liver.

ANTIAMOEBIC AND OTHER ANTIPROTOZOAL DRUGS

60.1 A 50-year-old gardner weighing 58 kg was admitted to the hospital with fever for 4 days, severe pain in right upper part of abdomen, loss of appetite, vomiting and marked weakness. He was not well for the past 2–3 weeks and had lost weight. There was no history of chronic diarrhoea. Palpation of abdomen revealed soft tender enlargement of liver 2 cm below costal margin. Marked tenderness was noted in the lower right intercostal region. Ultrasound showed a solitary 2.5 cm diameter abscess with sharp margins in the right lobe of liver. Stool examination was negative for any kind of ova and cysts. A clinical diagnosis of amoebic liver abscess was made and he was treated with:

Injection Metronidazole 500 mg i.v. over 1 hour every 8 hours for 5 days along with infusion of glucose-saline and vitamins. The fever and vomiting subsided and he started eating food. The injections were substituted by oral metronidazole 800 mg 3 times a day for another 5 days, and the patient became well, except weakness and mild tenderness in the right lower chest. Repeat ultrasound showed abscess cavity size to decrease to 1.5 cm. The patient was discharged with advise for vitamins and food.

(a) Was the choice of medication and route correct, or a better drug/route of administration is available?

(b) Should metronidazole therapy be extended or a repeat course given?

(c) Should the patient be given any other antiamoebic medication in addition to or following metronidazole?

(*see* Appendix-1 for solution)

SOLUTION 60.1

SOLUTION 60.1

a. Metronidazole is the drug of choice for amoebic liver abscess. Tinidazole is an equivalent, but not necessarily better alternative. Since the patient was seriously ill and was vomiting, the initial choice of i.v. route of administration was appropriate. It was correctly changed to oral route once the patient improved, because oral bioavailability of metronidazole is nearly complete.

b. Experience has shown that a single 10-day course of metronidazole is generally enough to kill all viable amoebae in the liver abscess, though the abscess cavity may persist for few weeks and heal spontaneously. Since the patient has improved clinically, visualization of persisting abscess cavity on ultrasound is not in itself an indication to extend/repeat metronidazole therapy.

Contd...

c. Since amoebic liver abscess is always secondary to colonization of colon by amoebae (which may be asymptomatic) and because metronidazole does not effectively eradicate cyst forming trophozoites from the colon (it is completely absorbed in the upper intestine, and very little reaches the colonic lumen), a luminal amoebicide should be given along with or after metronidazole. Absence of cysts in stools does not ruleout colonization of colon by amoebae. The first choice luminal emoebicide that should have been given in addition is:

Diloxanide furoate 500 mg 3 times a day for 5–10 days alongwith or after metronidazole.

ANTHELMINTIC DRUGS

61.1 A 40-year-old male weighing 60 kg presented with history of 2 episodes of sudden onset fits over the past 3 days. There is no past history of fits or any nervous disorder. The patient has been having headache for the last one month or so which responds to paracetamol. His wife who witnessed the fits gave a description which fitted tonic-clonic seizures. The wife also informed of noticing some behavioural changes for the last 2 months. The fits were followed by confused behaviour and drowsiness for 2–3 hours. There is no family history of fits or mental illness. MRI scan of the brain revealed 4 active cortical parenchymal cysticerci. A diagnosis of neurocysticercosis was made.

(a) Should this patient be treated with specific anthelmintic drug, or only symptomatic treatment of seizures is indicated?

(b) If anthelmintic therapy is to be given, should antiseizure drug also be given? If both are to be given, should they be given concurrently or one after the other or in overlapping manner starting with one first? What should be the sequence?

(c) If anthelmintic is to be given, which drug, dose and duration of treatment would be appropriate and why?

(d) Whether any other medication needs to be given? If so which, when, how long and why? (*see* Appendix-1 for solution)

SOLUTION 61.1

SOLUTION 61.1

a. This patient of neurocysticercosis is suitable for treatment with anthelmintic drug, because there are multiple active parenchymal cysticerci in the cerebral cortex which in addition to seizures can cause other focal reactions in the brain. Planned killing of the cysticerci under corticosteroid cover may prevent future episodes of the reaction and may abolish the cause of seizures, so that long term antiseizure therapy can be avoided.

b. The seizures must be controlled first before starting anthelmintic treatment. The preferred drug is carbamazepine; start with 200 mg 3 times a day, increase by 200 mg/day if the seizures recur till they are fully suppressed or a maximum of 1200 mg/day dose is reached. A second antiseizure drug may be added in nonresponsive cases. However, most cases respond to carbamazepine alone. It should be continued during the course of anthelmintic medication and for about 6 months thereafter, followed by gradual withdrawal over another 2–3 months.

c. Albendazole is the anthelmintic of choice in neurocysticercosis. To this patient, it should be given in a dose of 400 mg twice daily with milk or fat-rich food (to enhance absorption) for 15 days. It is better than the alternative drug praziquantel, because cure rate with albendazole is higher and praziquantel needs to be given for longer period (15–30 days). Carbamazepine induces praziquantel metabolism and lowers its blood level, but not that of albendazole. Dexamethasone (which has to be given) also lowers praziquantel blood levels, but increases albendazole absorption.

d. Dexamethasone in a dose of 8–12 mg once daily in the morning should be started 2 days before initiating albendazole, continued throughout the course and till 15 days thereafter, followed by gradual tapering of dose and final withdrawal. This is essential to suppress the inflammatory reaction to the dying cysticerci killed by albendazole therapy.

October, 2016.